MEDICAL LIBRARY

SEP 23 1947

VOLUME 74 NUMBER 2

AMERICAN JOURNAL

OF

DISEASES OF CHILDREN

EDITORIAL BOARD

CLIFFORD G. GRULEE, Chief Editor
Box 671, Evanston, Ill.

OSCAR M. SCHLOSS, New York
FRITZ B. TALBOT, Boston
A. A. WERCH, Cincinnati
H. F. HELMHOLZ, Rochester, Minn.
FRANCIS SCOTT SMYTH, San Francisco
JAMES L. WILSON, Ann Arbor, Mich.

AUGUST 1947

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second Class matter Jan. 4, 1911, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

COPYRIGHT, 1947, BY THE AMERICAN MEDICAL ASSOCIATION

CONTENTS OF PREVIOUS NUMBER

JULY 1947. NUMBER 1

Cerebral Damage in Infants and in Children: Some Observations on Its Causes and the Possibilities of Its Prevention. Harold K. Faber, M.D., San Francisco.

Early Immunization Against Pertussis. J. M. Adams, M.D.; A. C. Kimball, Ph.D., and F. H. Adams, M.D., Minneapolis.

Oral Administration of Penicillin in Pediatrics. Henry A. Reisman, M.D., Jamaica, N. Y., and Arthur A. Goldfarb, M.D., and Molly Molloy, M.S., New York.

Syndromes of Kerosene Poisoning in Children. Matthew M. Steiner, M.D., Chicago.

Secondary Pneumonitis. Peter V. Vajdafi, M.D., Budapest, Hungary.

Factors Influencing Retention of Nitrogen and Calcium in Period of Growth: VII. Effect of Methyl Testosterone. Joseph A. Johnston, M.D., Detroit.

Case Reports:

Islet Cell Tumor of Pancreas in a Newborn Infant (Nesidioblastoma). Harry Sherman, M.D., Brooklyn.

Diphtheria of the Esophagus: A Case Involving Stomach and Tongue. Archibald L. Hayne, M.D., Chicago.

News and Comment.

Abstracts from Current Literature.

Book Reviews.

Directory of Pediatric Section.

American Journal of Diseases of Children

VOLUME 74 AUGUST 1947 NUMBER 2

COPYRIGHT, 1947, BY THE AMERICAN MEDICAL ASSOCIATION

ASYMMETRIC SPASTIC INFANTILE CEREBRAL PALSY

A Clinical Study of Its Causation

JOHN McGOVERN, M.D.
AND
HERMAN YANNET, M.D.
SOUTHBURY, CONN.

THE TERM "infantile spastic cerebral palsy" is generally applied to spastic motor defects, with or without athetosis, recognized at birth or soon after or developing during the early years of life, and due to abnormalities of the brain. The vast majority of these cases fall into the following etiologic categories: (1) developmental anomalies, which in a small number may be genetically determined; (2) cerebral trauma during the birth process; (3) cerebral degenerations, and (4) acquired postnatal cerebral abnormalities, mainly traumatic or infectious. The clinical picture may be rather variable, but in general can be separated into two groups: (1) the symmetric palsies, including the diplegias, which exhibit symmetric involvement on both sides of all four extremities but to a greater degree in the legs, and the paraplegias, in which the lower extremities are equally involved, and (2) the asymmetric palsies which include the hemiplegias, monoplegias, triplegias and quadriplegias. The quadriplegias differ from the diplegias in that all four extremities are more or less irregularly involved with equal or greater spasticity in the arms.

The relative importance of the various causal factors mentioned in the over-all problem of the infantile spastic cerebral palsies has been the subject of considerable clinical and pathologic investigation. The older writers, in the main, favored the concept of birth trauma, through cerebral hemorrhage, asphyxia or circulatory interference, as the most important causative factor. During the last twenty-five years, the importance of prenatal factors leading to developmental anomalies has been stressed. At the present time, one may summarize the prevailing view as follows: that, while increasing importance is being given to the influence of prenatal factors, at present mostly unknown, in the causation of the symmetric palsies, abnormal events occurring during the birth process are considered of prime importance in the causation of the asymmetric palsies.[1]

From the Southbury Training School, Southbury, Conn., and the Department of Pediatrics, Yale Medical School, New Haven, Conn.

(Footnotes continued on next page)

In a recent clinical study by one of us[2] evidence was presented suggesting that in both the spastic diplegias and the asymmetric cerebral palsies the possibility of developmental cerebral defects must be considered as of major causal importance.

The present study is concerned with a more detailed clinical analysis of a larger group of cases of asymmetric spastic cerebral palsy. The plan of study was designed further to investigate the relative importance of birth trauma and prenatal factors in the causation of this condition.

Since the opening of the Southbury Training School in October 1940, there have been admitted a total of 127 patients with spastic cerebral palsy for whom reasonably accurate and complete histories could be obtained to allow satisfactory clinical evaluation. Of this group, 52, or 41 per cent, had diplegia, 7, or 6 per cent, paraplegia (5 of the 7 had paraplegia of the familial type) and 68, or 54 per cent, were asymmetrically involved. The present study is confined to the last group, primarily.

The historical data for the analysis were obtained, as in the previous study, from three sources; namely, personal interviews with parents or guardians, home visits by trained social service workers and records from hospitals and institutions in which the patients were previously confined.

RESULTS

Table 1 shows the distribution of cases according to cause and type of neurologic defect. The diagnosis of birth trauma was strictly confined to those cases exhibiting the following 2 historical criteria: (1) labor

TABLE 1.—*Distribution According to Cause and Nature of Palsy*

Cause	Hemiplegia	Quadriplegia	Triplegia	Monoplegia	Total
Birth trauma	8	3	..	1	12 (18%)
Postinfectious	5	4	..	2	11 (16%)
Rhisoimmunization	..	7	..	..	7 (10%)
Brain tumor	1	..	..	..	1 (1%)
Undifferentiated	28	6	1	1	36 (54%)
Total	42 (63%)	20 (30%)	1 (1%)	4 (6%)	67 (100%)

was abnormally long, difficult or complicated, and (2) the immediate postnatal period was stormy, with delay in initiation of respirations, cyanosis and signs of irritation of the central nervous system, such as excessive drowsiness or convulsive phenomena. In all cases the impres-

1. Benda, C. E.: Late Effects of Cerebral Birth Injury, Medicine **24**:71, 1945. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, Springfield, Ill., Charles C Thomas, Publisher, 1937. Grinker, R. R.: Neurology, ed. 2, ibid., 1937. Wilson, S. A. K.: Neurology, edited by A. N. Bruce, Baltimore, Williams & Wilkins Company, 1940.

2. Yannet, H.: Etiology of Congenital Cerebral Palsy, J. Pediat. **24**:38, 1944.

sion of birth trauma was indicated by the attending physician at the time of birth. It is appreciated that cranial hemorrhages or other vascular accidents have been recorded after essentially uncomplicated deliveries. Since the data were to be used for comparative purposes, it was felt that the more rigid the diagnostic criteria, the more justifiable would be the resulting conclusions. On this basis, a diagnosis of birth trauma was made in 18 per cent of the cases of asymmetric palsy, the larger number of cases being of hemiplegia. In the cases of postinfectious palsy, which accounted for 16 per cent, there were 2 cases of epidemic cerebrospinal meningitis (meningococcic), 2 cases of encephalitis due to pertussis and 7 cases of nonspecific nonsuppurative encephalitis. In most of the cases the infection occurred before the first year in children who, as far as can be determined, were developing in a normal fashion. Of the 7 cases of Rh isoimmunization or kernicterus, representing 10 per cent of the group, 6 have been previously reported in detail.[3] The seventh was similar in clinical and serologic aspects. All exhibited quadriplegia. There was 1 case of astrocytoma in a child in whom early signs of hemiplegia developed toward the end of the first year of life and who was operated on successfully at 6 years. The undifferentiated cases included those in which no definite causal diagnoses could be made. These cases would be ordinarily classified by us as developmental defects. In no case was the diagnosis of degenerative cerebral disease made. This can be explained, in part, by the fact that the average age of the group was well past 25 years, and that the commonest types of degenerative cerebral processes usually are fatal early in life.

Hemiplegia, occurring in 63 per cent of the total group, was the commonest manifestation. It is of interest that in only 2 (15 per cent) of the 13 cases of acquired palsy did right-sided involvement occur (birth trauma [1 case] and postinfectious [1 case]), as compared with 18 of the 28 cases in the undifferentiated group (64 per cent), which is a statistically significant difference. Expressed in another way, of the 20 cases of hemiplegia on the right side in the entire group only 2 (10 per cent) occurred in patients who acquired their cerebral abnormality as a result of birth trauma or infection. Kernicterus was the commonest diagnosis for the patients with quadriplegia, accounting for 30 per cent of the cases in this group.

The following tables have been prepared in order to determine whether the cases definitely diagnosed as birth trauma exhibit a characteristic profile. If so, this might help in the evaluation of the possibility that among the undifferentiated group there may have been an appreciable number of children injured at birth who, however, did not meet the rigid criteria set for the diagnosis of birth trauma. Pertinent data

3. Yannet, H., and Lieberman, R.: Central Nervous System Complications Associated with Kernicterus, J. A. M. A. **130**:335 (Feb. 9) 1946.

in the family histories, past histories and physical examinations for the group with birth trauma and the undifferentiated group are summarized and compared. Similar data from a previous paper pertaining to the spastic diplegias are also included for comparative purposes. The data in the latter group had strongly confirmed the belief that the diplegias represent the results of congenital cerebral developmental defects.[2]

Table 2 summarizes certain pertinent factors in the family histories. It will be noted that in the group with birth trauma 83 per cent of the children were first born as compared to 39 per cent in the undifferentiated group. The Connecticut registration report [4] for 1925 (approximately the average year of birth of these children) showed that 36 per cent of the children born in Connecticut that year were first born. The difference between the expected and the actual incidence of first born for the birth trauma group is highly significant and agrees with the

TABLE 2.—*Summary of Pertinent Factors in Family Histories*

	Asymmetric Palsy		Spastic Diplegia (47)
	Birth Trauma (12)	Undifferentiated (36)	
Maternal age (years)	27.0 ± 2.0*	31.0 ± 1.5	28.6 ± 0.7
Proportion first born	83.3%	39.4%	38%
Proportion later born (4+)	8.3%	39.4%	38%
Mean birth rank	3.3 ± 0.3	3.2 ± 0.5	3.1 ± 0.2

* Standard error.

well recognized hazard of primogeniture as regards birth injuries. The incidence of first born in the undifferentiated group is not abnormal.

The younger mean maternal age at the time of birth of the affected child in the birth trauma group is expected in view of the higher incidence of first born in this group. The mean maternal age in the undifferentiated group (31.0 plus or minus 1.5 years), however, is significantly greater than the expected mean maternal age as calculated from the report of the Connecticut Bureau of Vital Statistics [4] for 1925 (27.3 years). The significance of advanced maternal age in relation to various abnormalities of development has been discussed in a previous paper.[2]

Table 3 summarizes the pertinent factors in the birth histories. Practically all pregnancies were uncomplicated. In less than half of all the cases was delivery in a hospital, with a slightly larger proportion in the group with birth trauma, as might be expected. Also, all the cases in which there was birth trauma were attended by physicians. An abnormal delivery was described in only 4 of the 36 undifferentiated cases. While no child was prematurely born in the group with birth trauma, 25 per cent of the undifferentiated group were said to be pre-

4. Registration Report, State of Connecticut, 1925, vol. 78.

mature (birth weight 5 pounds [2,268 Gm.] or less). Because so small a number in this group was delivered in hospitals, the accuracy of this observation is debatable. However, compared with similarly obtained data from other types of patients admitted to the institution, the incidence may be considered as definitely abnormal. In this respect, the cases of undifferentiated asymmetric palsy resemble those of spastic diplegia.

TABLE 3.—*Summary of Pertinent Factors in Birth Histories*

	Asymmetric Palsy		Spastic Diplegia (47)
	Birth Trauma (12)	Undifferentiated (36)	
Pregnancy uncomplicated	100%	92%	98%
Born in hospital	58%	35%	15%
Physicians in attendance at home birth	100%	69%	60%
Abnormal delivery	100%	11%	1%
Incidence of prematurity	.....	25%	13%

Table 4 summarizes the pertinent clinical features. While the patients with undifferentiated asymmetric palsy were somewhat older, the mental levels were essentially the same. It must be stressed that our groups represent children who in addition to the motor defect also exhibit a severe degree of intellectual impairment. Males were slightly more numerous in both groups although not significantly so. The circumference of the head in the group with birth trauma was significantly

TABLE 4.—*Summary of Clinical Features*

	Asymmetric Palsy		Spastic Diplegia (47)
	Birth Trauma (12)	Undifferentiated (36)	
Age (years)	22.8 ± 4	28.8 ± 2	22.5
Mental level (I. Q.)	33 ± 7	35 ± 4	24
Males	58%	56%	50%
Circumference of head (cm.)	50.8 ± 0.7	52.8 ± 0.5	50.0
Incidence of convulsive disorders	67%	79%	37%
Incidence of congenital anomalies	....	9%	30%

smaller than in the undifferentiated group. The range of circumferences of the head was about the same in each group, being approximately 47 to 57 cm., with the curve shifted to the left in the cases of birth trauma, as the averages indicate. The incidence of convulsive disorders was extremely high in both groups (they were found in almost 75 of all the cases). In the group with birth trauma, the 8 cases with convulsive disorders included all the patients with hemiplegia, whereas none of the patients with quadriplegia exhibited this condition. The significance

of this observation from a neurologic viewpoint is not apparent. There were 3 cases of associated noncerebral congenital defects in the undifferentiated group. This included 1 case of torticollis, 1 case of bilateral cataracts and 1 case of congenital heart disease. Associated noncerebral congenital defects were not noted in the group with birth trauma.

A review of the preceding tables, as well as other facts given, indicates the suggestive similarity of many of the observations in the undifferentiated group to those previously described for the spastic diplegias. On the other hand, the dissimilarity of the observations in the group with birth trauma from those in the undifferentiated group are equally evident. These differences include: (1) the high proportion of first born in the group with birth trauma; (2) the significantly advanced

TABLE 5.—*Cases of Undifferentiated Cerebral Palsy Divided into Subgroups According to Size of Head, Material Age, Birth Rank, Prematurity and Side Involved*

Group	No.	Mental Level (I. Q.)	Maternal Age, Years	Mean Birth Rank	First Born, %	Size of Head, Cm.
I. Size of Head						
Large	22	36	30.7 ± 0.5	2.5 ± 0.3	45	54.0 ± 0.3
Small	14	38	31.1 ± 2.8	3.0 ± 1.4	36	49.8 ± 0.8
II. Maternal Age						
Advanced	15	36	38.8 ± 0.9	4.9 ± 0.9	20	52.3 ± 0.8
Young	15	42	23.9 ± 1.2	1.9 ± 0.4	60	53.1 ± 0.6
III. Birth Rank						
First born	12	41	25.8 ± 2.4	1.0	100	53.0 ± 0.4
Later born	18	37	35.1 ± 1.6	4.9 ± 0.7	0	52.8 ± 0.8
IV. Prematurity						
Premature	9	30	32.3 ± 2.9	2.4 ± 1.2	45	52.8 ± 0.4
Full term	23	42	30.6 ± 1.2	3.0 ± 0.3	39	52.5 ± 0.3
V. Side Involved (Hemiplegia)						
Right	18	44	29.4 ± 1.7	2.7 ± 0.5	41	52.6 ± 0.4
Left	10	32	32.0 ± 2.8	2.4 ± 1.0	50	53.0 ± 0.7

maternal age in the undifferentiated group; (3) the smaller average size of head in infants with birth trauma; (4) the increased incidence of prematurity in the undifferentiated group, and (5) the tendency for the hemiplegia in the group with birth trauma to involve the left side, an observation also true for the other cases of acquired cerebral palsy, the cases of postinfectious palsy, as compared to the major tendency to right-sided involvement in the undifferentiated group. The results of the study, so far, therefore suggest that, as regards causation, the undifferentiated group represents a separate category, different from that in which birth trauma was causative. We substantiated this by a further analysis of the undifferentiated group, utilizing the individual points already listed that served to characterize the group with birth trauma.

Table 5 summarizes the results of this analysis. Using each critical factor, we divided the undifferentiated group into two separate groups representing the relative extremes. The levels used for making the

divisions were arbitrarily chosen to divide the group into two subgroups of reasonable size to allow statistical study. The point of division for size of head was 53 cm. and for maternal age was 32 years. The pertinent data for each of these subgroups were averaged to determine the degree of homogeneity in the group as a whole. Thus, with head size as the critical factor, the 36 cases in the undifferentiated group were divided into cases with circumference of head less than 53 cm. and cases with circumference 53 cm. or above. The average size of head in one group was 54 cm., and in the other was 49.8 cm. A comparison of these two groups yielded no significant differences as regards the other critical factors. Similarly, separation on the basis of maternal age, birth rank, prematurity and, as regards hemiplegia, the side involved, showed no significant differences. One may draw the conclusion from this that, as regards those factors which we have shown tend to characterize the cases with birth trauma, the undifferentiated group was essentially homogeneous. It would thus appear unlikely that the undifferentiated group included any appreciable number of patients whose cerebral abnormality could be related to accidents during birth.

COMMENT

Our data indicate the relative importance of various causal factors in a group of cases of infantile spastic cerebral palsy with asymmetric involvement. It is important to stress that the group studied, in addition to the specified neurologic defect, exhibited a pronounced degree of mental retardation. Whether a similar distribution of causes will be demonstrated in children with similar neurologic involvement but of normal or only slightly retarded intelligence remains to be seen.

The data also suggest one of the possible causes for the disagreement so frequently seen in the literature on the relative importance of various factors in the causation of infantile spastic cerebral palsy. The latter term, as previously indicated, includes a wide variety of neurologic abnormalities. The relative importance of various causative factors in any group of cases of infantile spastic cerebral palsy will depend on the distribution of these neurologic types in the group as a whole. It will undoubtedly also depend on the age distribution and, as indicated earlier, probably the incidence of various intellectual levels. The data in this and the preceding paper [2] indicate this point as regards the distribution of neurologic types. Thus a diagnosis of unknown causation (i. e. undifferentiated and presumably developmental) was made in 30 per cent of the cases of quadriplegia, 67 per cent of the cases of hemiplegia and 100 per cent of the cases of diplegia. A definite diagnosis of Rh isoimmunization (kernicterus) as the cause of the spastic palsy was made in 35 per cent of our cases of quadriplegia but in none of the other varieties of neurologic defects. In fact, this was the commonest cause for quadri-

plegia in our group, being over twice as important as birth trauma. On the other hand, the incidence of birth trauma was about the same in the cases of hemiplegia and quadriplegia, namely, between 15 and 20 per cent.

Our total group of 127 cases may be considered fairly representative of infantile spastic cerebral palsy associated with relatively severe mental defect, evaluated when the patients were about 20 to 25 years of age. With these qualifications, it is of interest that in only 31 cases (24 per cent) was a definite diagnosis of an acquired cerebral defect made, and in only 9 per cent of these could the defect be attributed to birth trauma. On the other hand, a diagnosis of "undifferentiated" was made in about 75 per cent of the cases.

The term "undifferentiated," as was indicated earlier, is actually used to refer to cases of unknown causation. That is, in spite of reasonably complete and accurate historical data, and detailed examinations, all necessary laboratory aids being used, a specific causal factor could not be identified. The possibility was recognized that there were included in this group some cases that should have been placed in the acquired category (i. e., birth trauma, infection, etc.) but were misdiagnosed. The most likely error would probably be the failure to recognize and diagnose as such, cases of birth trauma with borderline birth and neonatal histories. We feel, however, that the data presented for the undifferentiated group make it unlikely that any significant number of cases have been so misdiagnosed. This is well shown by the persistent homogeneity exhibited by the undifferentiated group when evaluated in terms of the various critical factors which were found to characterize the cases of birth trauma including birth rank, maternal age, size of head, prematurity and the side involved in hemiplegia. An obvious corollary to this involves the conclusion that in the older, seriously defective person with asymmetric spastic cerebral palsy, a causal diagnosis of birth trauma is valid only in the presence of a definite history of abnormally difficult delivery associated with symptoms during the early neonatal period compatible with cerebral injury.

The data can be best interpreted as indicating the major importance of prenatal factors leading to developmental cerebral defects in the causation of asymmetric infantile spastic cerebral palsy. It is not intended to minimize the importance of birth trauma in this group but to help establish its relative position in the evaluation of the various causal factors involved.

SUMMARY

A group of 67 cases of infantile spastic cerebral palsy with asymmetric neurologic involvement and marked mental defect is reviewed. The clinical data were analyzed to help evaluate the relative importance of various causal factors. The group in which a definite history com-

patible with the diagnosis of birth trauma was present was shown to differ in many respects from the undifferentiated group in which this history was absent. These differentiating factors include: (1) the high proportion of first born in the group that experienced birth trauma; (2) the significantly advanced age of the mothers at the time of birth of the patients in the undifferentiated group, (3) the smaller average head size in the group which experienced birth trauma, (4) the increased incidence of prematurity in the undifferentiated group and (5) the tendency for hemiplegia in the undifferentiated group to involve the right side while hemiplegia on the left side occurred in practically all cases of palsy due to birth trauma as well as of postinfectious palsy.

The data were interpreted to indicate that the undifferentiated group, which represented 54 per cent of the total number of cases of asymmetric spastic paralysis, have many features in common with the spastic diplegias and probably represent the result of prenatal conditions leading to developmental cerebral defects.

AN EPIDEMIC OF DIPHTHERIA

WILLIAM A. REILLY, M.D.
SAN FRANCISCO

THE GRADUAL loss of immunity to diphtheria in the United States among adults has been progressing, while the morbidity has been falling off. This has been going on since about 1915, when diphtheria prophylaxis in the United States was started. The effect was demonstrated when the American military forces went to Europe, where they were exposed perhaps to many more carriers, cases and different strains than in the United States.

This report deals with 216 patients who entered the 59th Evacuation Hospital in Palermo, Sicily, between August 1943 and May 1944. One hundred and thirty-five have been labeled as carriers, and 81 as having toxic diphtheria, though, as will be explained later, some of the former probably also were suffering from diphtheria.

The 413 personnel of the 59th Evacuation Hospital were from all parts of the United States. They served as a partial control for previous susceptibility to diphtheria and for some of the problems encountered with the epidemic. Twenty-four per cent of the personnel had positive Schick reactions; twenty years previously, one would have expected about 15 per cent to have positive reactions. This liability to diphtheria was probably due to increased prophylaxis, with its temporary active immunity, and the diminished contact with patients or with carriers, again because of prophylaxis and control measures of isolation, which have been widespread and early. Seventeen of the personnel presented problems of diphtheria.

The use of tellurite mediums for culture and of dextrose, sucrose and dextrin sugars for fermentation reactions and intracutaneous injections into guinea pigs (the Zingher-Soletsky modification of the Neisser method) for virulence were the procedures for testing these problems. Individual patients were often retested at twenty-four to forty-eight hour intervals during their illness and always during a carrier state; thus checks on laboratory observations were abundant. At the same time, my colleagues and I had to test similarly the contacts, as many as 1,000 daily. Our meager laboratory facilities were heavily strained early and the problem was only handled by supplementary help from the bacteriologic department of the University of Palermo Medical School.

where our hospital was situated. Schick tests were frequently done, as will be described later.

Of the 216 persons admitted, 81 had active diphtheria and 135 were classified as carriers; of the latter 19 were healthy carriers and 116 were carrying coincidentally, we thought, during infections of the upper respiratory tract, probably primarily caused by other organisms. Carriers were called healthy when they did not reveal active infection in the respiratory tract; some were food handlers; others, for instance, had hepatitis or wounds with only a sore throat subjectively, with slight fever and/or contact with diphtheria. Those carriers with active infections of the respiratory tract coincidentally carrying diphtheria bacilli were a trying problem for diagnosis and treatment. Confronted with an early infection characterized, as types, by follicular tonsillitis or a red, swollen pharynx, both with positive cultures and a positive Schick reaction, one was hard put to decide definitely that this would not develop into membranous toxic diphtheria—all the more so when the

TABLE 1.—*Relationship Between Schick Reactions and Diphtheria in Four Hundred and Thirteen Personnel of 59th Evacuation Hospital*

Schick Reactions	Negative 314 (76%)	Positive 99 (24%)
Number with diphtheria problem	11	6
With disease	4	5
Carrier	7	1

results of the fermentation and virulence tests were reported as positive three to five days later. Antitoxin was given to all of these with a positive Schick reaction. Patients were hospitalized on the first or second day of their disease and were given a Schick test at that time; the test was interpreted at least forty-eight hours later. Thus we had the relative safety of seeing the patient early in the disease. Because so frequently positive cultures and fermentation and virulence reactions were found in this type of "carrier," Schick tests were done on many as a basis for the use of antitoxin. Twenty-nine (35 per cent) of 116 tested had positive reactions. It was routine to isolate all patients with disease of the upper respiratory tract, to make cultures and to give them Schick tests, so prevalent was the diphtheria organism in various units of the Army.

By "active diphtheria" is meant membraneous lesion, toxicity, positive cultures and fermentation and virulence reactions for the diphtheria bacillus.

Various problems were encountered, and some are herein described and discussed.

I. THE OCCURRENCE OF ACTIVE DIPHTHERIA IN PERSONS WITH NEGATIVE SCHICK REACTIONS

There were 13 patients with active diphtheria whose Schick reactions were negative; 10 received antitoxin and 3 did not. There were no deaths; there was one complication—short-lived myocarditis—in a patient treated adequately with antitoxin. Among those with active infections of the upper respiratory tract carrying virulent diphtheria, there were 6 negative reactors of whom 3 received antitoxin and 3 did not; there were no deaths or complications.

To some this would seem an impossibility—the acquisition of active diphtheria in the presence of a negative Schick reaction. At one time a negative reaction meant that there was at least $\frac{1}{60}$ to $\frac{1}{40}$ unit of antitoxin per cubic centimeter of serum; recent measurements,[1] however, indicate that the range of antitoxin content of blood for a negative reactor is between only $\frac{1}{500}$ and $\frac{1}{250}$ unit per cubic centimeter of blood—a much smaller amount and not sufficient to prevent active diphtheria from certain strains. This is especially true of the gravis strains. The accepted Schick immunity level is not quite high enough to protect a population against gravis infections at their worst, but is an efficacious measure in the majority of outbreaks of diphtheria.[2] On a tellurite blood medium, organisms were tested to determine the types —gravis, intermedius and mitis. The frequency of the types which we were dealing with was in this order: gravis, mitis, intermedius. Unfortunately I cannot now state the types associated with the 16 cases herein mentioned in which the Schick reaction was negative, for these data went with the patient as he was evacuated.

These patients did not have negative reactions because of cachexia or malignant diphtheria. That this Schick material was reliable was attested by the finding of positive reactions among other patients on the same day of reading as among the negative reactors. The tests were read between forty-eight and seventy-two hours after the material was given intracutaneously. It was not safe to wait longer for the possible late development of a positive reaction, nor did we have the facility of confirmation by quantitative measurement of the antitoxin content by the Kellogg test.

That negative Schick reaction may not indicate sufficient immunity is a possibility. A quantitation of antitoxin by the Kellogg procedure

1. Jordan, E. O., and Burrows, W.: Textbook of Bacteriology, ed. 13, Philadelphia, W. B. Saunders Company, 1941, p. 476.

2. Anderson, J. S.; Happold, F. C.; McLeod, J. W., and Thomson, J. G.: On the Existence of Two Forms of Diphtheria Bacillus—B. Diphtheriae Gravis and B. Diphtheriae Mitus—and a New Medium for Their Differentiation and for Bacteriological Diagnosis of Diphtheria, J. Path. & Bact. **34**:667-681 (Sept.) 1931.

would be a more exact measure than the rougher approximation by the Schick test. It is rather difficult, nevertheless, to understand the discrepancy of negative Schick reaction, because 1 unit of diphtheria antitoxin neutralizes one hundred lethal doses of toxin in a 250 Gm. guinea pig. In the human being so little toxin per hour is produced that it is difficult to understand why this small amount of toxin should not be neutralized by the humoral antibodies of those with negative Schick reactions. Also, in experimental disease the whole amount of toxin enters the body in a few seconds.

Schick [3] theorized that occasionally something interferes with the interaction of toxin and antitoxin at the site of entrance of the toxin—the diphtheria bacillus. Certainly virulent bacilli can live locally in healthy carriers. In the case of these persons with negative Schick tests who had diphtheritic disease, one might postulate that the bacillus is the factor interfering with the neutralization mechanism.

TABLE 2.—*Rates of Diphtheria in Immune and Nonimmune Persons, 1932 to 1935, in Cork, Leeds, Manchester and Stafford*

	Total Cases	Percentage of All Cases	Percentage Fatal, Severe
Gravis	2,108	5.1*	2.4*
Intermedius	815	2.5*	1.1*
Mitis	961	1.3*	0.2*

* Patients immunized.

Occurrence of active diphtheria in those with negative Schick tests has been variously estimated at between 2 and 5 per cent. In 1936, Cooper and his colleagues [4] gave a good over-all estimate of this incidence in the British Isles, as in table 2. Thirteen (16 per cent) in our group of 81 cases of active diphtheria is a much higher incidence than hitherto reported.

II. THE BEHAVIOR OF DIPHTHERIA IN A PERSON WITH A POSITIVE SCHICK TEST

We had 19 nonimmune persons who were given antitoxin early and in adequate doses. No deaths occurred. There was only one complication, serum sickness, of course not due to the disease.

Eight other nonimmune persons were not treated with antitoxin, and no deaths occurred, but myocarditis developed in 1. These were virulent strains; we did not determine always whether they were of the gravis type.

3. Schick, B.: Personal communication to the author.

4. Cooper, K. E.; Happold, F. C.; McLeod, J. W., and Woodcock, H. E. de C.: Review of Observations Which Have Accumulated with Regard to Significance of Diphtheria Types in the Last Four-Five Years, 1931-1935, Proc. Roy. Soc. Med. 29:1029-1054 (July) 1936.

These carriers resulted: 2 treated with antitoxin and 1 not given antitoxin, without deaths or complications.

Diphtheria occurring in nonimmune persons may cause fatality, complications or immunity, depending on the ability of the host to generate antibodies and the virulence and strain of the organism. The ability to generate antibody implies particularly the speed as well as the amount, so that if sufficient antitoxin is quickly generated by a patient

TABLE 3.—*Diphtheria in Persons with Positive Reactions to the Schick Test Who Had Active Disease*

	With Active Disease		Carriers	
	Yes	No	Yes	No
Antitoxin.....	19	8	2	1
Complications.....	1	1	0	0

he will neutralize the toxin of his diphtheria bacillus and not be killed or perhaps not suffer complications.

III. THE INFLUENCE OF SULFONAMIDE DRUGS ON THE DISEASE AND THE CARRIER STATE

All of the persons in table 4 had active disease (the carriers included), all had virulent strains with two possible exceptions (cases 2 and 6 of table 4, the records of which were unavailable) and all had negative

TABLE 4.—*Influence of Sulfonamide Drugs on the Disease and the Carrier State*

Case	Disease	Carrier	Fermentation and Virulence Reactions	Duration of Disease or Carrier State After Start of Sulfonamide Therapy, Days	Drug Used
1	+	..	+	11	Sulfadiazine
2	+	..	No record	17	
3	+	..	+	8	
4	+	..	+	12	
5	+	..	+ mitis	12	
6	..	+	No record	4	Sulfathiazole
7*	..	+	+	12	
8	..	+	+ mitis	14	

* This patient was not cured by the sulfonamide treatment.

reactions to the Schick test before treatment. Whether by chance or foresight, we did not use sulfonamide drugs for those with positive reactions.

Sulfathiazole and sulfadiazine were the only two sulfonamide drugs used. The figure in days in table 4 covers the period between the starting of the treatment with the drug and the obtaining of the first of three negative cultures at twenty-four to seventy-two hour intervals. No antitoxin was given.

Appraising the effect of the sulfonamide compounds with this small test group, it is seen that there are 4 fair examples (cases 1, 3, 4 and 5 of table 4) and 1 questionably fair example (case 2 of table 4), of the cure of the disease by sulfadiazine, and 2 fair examples (cases 7 and 8 of table 4) and 1 questionable example (case 6 of table 4—fermentation and virulence reactions unknown) of eradicating the carrier state.

Sulfonamide drugs, especially sulfathiazole and sulfadiazine, in our experience, eradicate secondary invading organisms and allow antitoxin, administered or generated by the host, to become more effective. We clinically satisfied ourselves of this effect by simultaneously treating another group with sulfonamide drugs and antitoxin.

Our limited experience with penicillin showed that in general it was effective in eradicating secondary organisms and occasionally the carrier state in diphtheria.

IV. HOW LONG DO MEMBRANES PERSIST AFTER ADEQUATE DOSES OF ANTITOXIN?

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
No. of cases	1	..	2	..	2	5	..	..	..	..	..	..	..	..	1	1

The foregoing sampling gives a rough determination of the duration of membranes, an average of six and one-half days, where we had data in our series. This is slightly longer than our past experience in the United States, and one wonders whether the secondary invaders lengthened this period, for simultaneous administration of sulfonamide drugs to another group of 4 patients caused membranes to disappear after four and one-half days.

V. INSTANCES OF THE PERSISTENCE OF POSITIVE SCHICK REACTIONS AFTER THE DISEASE AND ADMINISTRATION OF ANTITOXIN

Two patients, each of whom received 40,000 units of antitoxin for a virulent diphtheria bacillus causing toxic diphtheria without complications, still had positive Schick reactions, one six weeks and the other nine weeks afterward.

Schick tests done within forty-eight hours of administering 25,000 to 75,000 units of antitoxin elicited negative reactions in all cases.

VI. DURATION OF THE CARRIER STATE

In this group of 117 cases for which we have data on the duration of the carrier state, it should be noted that the day or week in the table indicates the time after onset when the first of three consecutive negative cultures at twenty-four to forty-eight hour intervals was obtained and that while cultures were positive they were repeated at twenty-four to forty-eight hour intervals with fermentation and virulence tests to substantiate a true or dangerous carrier state.

TABLE 5.—*The Duration of the Carrier State*

Healthy Carriers																										
Day after onset when first negative culture was obtained...	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15-20	20-35	45-50									
Number of cases	..	5	3	2	..	2	1	..	..	..	1	1	1	1	1	1	..									
Carriers with Infections of the Upper Respiratory Tract																										
Number of cases	2	1	6	9	8	..	7	1	2	..	1	1	1	..	3	..	1									
Active Diphtheria																										
Days after onset when first negative culture was obtained.....	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Number of patients given antitoxin																										
Schick test positive	1	..	3	..	..	..	1	..	1	..	..	..	..	1												
Schick negative	..	..	1	1	..	..	1	..	..	1	1	..	..	..	1	..	2									
No records	3	..	1	..	1	1	1	..	4	..	1	..	1	2	..	2	..	..	..	..	1+	1	1	..	1	1
Not given antitoxin																										
Schick positive	..	1	..	1																						
Schick negative	..	..	..	1																						
No records																										
Weeks after onset when first negative culture was obtained.....	5	6	7	8	9	10	11	12	13																	
Number of patients given antitoxin																										
Schick positive	2+	..	..	1	1																					
Schick negative	..	2	..	1																						
No records	2+	2																								
Not given antitoxin																										
Schick positive																										
Schick negative	1																									
No record																										

All patients had two more negative cultures after the first; + indicates that the patient was transferred to another hospital, still a carrier.

The healthy carriers (19) carried for an average of eight days; one who carried for twenty-two days may have had active diphtheritic disease also. Healthy carriers may carry for a few days to a few weeks. A small percentage may become chronic carriers; we had one who was so for over three months.

Those carrying diphtheria bacilli during infections of the upper respiratory tract (43) did so for an average of seven days, about the same time as did the healthy carriers. This is more evidence leading us to feel that these infections of the upper respiratory tract may not have been primarily due to diphtheria but that the presence of the diphtheria bacillus may have been coincidental, even though often virulent and necessitating administration of antitoxin to those with positive reactions to the Schick test. Such patients were a trying clinical problem, as stated earlier. The clinical adage, "In cases of suspected diphtheria give antitoxin and do not wait for laboratory confirmation," was reversed here, for clinically these patients did not have membranes, the usual toxicity, etc., but repeated cultures showed the existence of virulent diphtheria bacilli.

Of the 55 patients with active diphtheria (membrane, toxicity, virulent diphtheria bacilli), for whom we have the data in the table, 50 were treated with antitoxin and 5 were not. The majority (34) were free of organisms twenty-one days after onset. This is about the same time, two to four weeks, reported by others for convalescent diphtheria. A small percentage became chronic carriers. Not included in table 5 because of lack of data are 1 patient who carried for four months, 1 for two and one-half months and 2 for two months—all while in our hospital. These and the ones marked with a plus sign in the table were evacuated, and the full duration of their carrier state was unknown to us.

Among patients with active diphtheria given antitoxin were 9 who previously had Schick reactions, 6 who had positive reactions and 19 who had not previously been given a Schick test. Among those not given antitoxin, it is interesting to note that 3 who previously had positive Schick reactions were free of bacteria five days after onset. There does not seem to be any significant difference in carrier time between those partially immune before (negative reaction to Schick test) and those not immune (positive reaction), nor does the antitoxin given to those two groups seem to have made any difference in duration of carrying the organism.

VII. DURATION OF VIRULENCE

Convalescent carriers often lost virulence of the type carried but they may continue to carry for some time thereafter an avirulent

diphtheria bacillus, or, as some name it, pseudodiphtheria bacillus. Here is a group of 17 such carriers, with the following characteristics: All patients had active diphtheria; all received antitoxin except 1 (case 3 of table 6); all had repeated negative reactions to the virulence test after the day recorded in the table. Thereafter, usually for several to ten days and uncommonly for longer times (case 8 of table 6 for twenty-four more days), they continued to carry avirulent diphtheria bacilli. They are included in the 55 cases of active diphtheria in the section "Duration of Carrier State," but the comparison of their tests for virulence (guinea pig) and carrier state (morphology and fermentations) was done more often and were frequently repeated after virulence was definitely lost.

TABLE 6.—*Duration of Virulence and Thereafter of Carrier State*

Case	Schick Reaction	Duration in Days of Virulence and Thereafter Carrier State	
		Virulence	Carrier State
1	Negative	16	19
2	Negative	35	36
3	Negative	30	35
4	Negative	42	50
5	Negative	42	60
6	Negative	43	45
7	Positive	8	34+ (mitis)
8	Positive	21	45
9	Positive	21	37
10	Positive	35	46
11	Positive	65+	65+
12	Positive	50+	50+
13	Test not done	19	19
14	Test not done	30	No data
15	Test not done	23	36
16	Test not done	56+	59+
17	Test not done	84+	84+ (mitis)

The plus sign means that the patient was transferred to another hospital still a carrier.

Testing for virulence and carrier states occasionally showed changes from positive to negative and back to positive before final unchanged negative reactions were found.

The partial immunity of those with negative reactions to the Schick test does not seem in general to have shortened the duration of virulence. Those with active diphtheria carried the bacilli longer than those with disease of the upper respiratory tract or healthy carriers, as was noted earlier in this report; likewise, virulence persisted longer in those with active disease.

SUMMARY

The increasing incidence of diphtheria among adults was indicated by an epidemic in the American army overseas. Seventy-six per cent of 529 adults had negative reactions to the Schick test; twenty years ago the expectancy of persons with negative reactions would have been 85 to 90 per cent. The reason for this diminished immunity is discussed.

Eighty-one patients with active diphtheria, 116 patients with disease of the upper respiratory tract due probably primarily to organisms other than diphtheria but who also were carrying virulent diphtheria bacilli and in whom diphtheritic membranes and toxicity often developed, and 19 healthy carriers were dealt with in the epidemic. The infections of the upper respiratory tract, mostly follicular tonsillitis or pharyngitis, when diphtheria membranes and toxicity developed became a trying diagnostic and therapeutic problem.

The number of those with negative reactions to the Schick test, 13 (16 per cent) of the 81 patients with active diphtheria, is much higher than heretofore recorded (2 to 5 per cent). Reasons for this are discussed.

Eight nonimmune patients were not treated with antitoxin. No deaths occurred, but myocarditis developed in 1 patient.

The frequency of the types of diphtheria organisms was probably in this order: gravis, mitis, intermedius, although the mortality was extremely low.

The possible favorable influence of sulfonamide drugs on the disease and the carrier state and of penicillin on the carrier state are described.

The duration of membranes of persons with positive reactions to the Schick test after diphtheria and the duration of carrier state and of virulence are described.

Helpful advice and criticism were furnished by Dr. J. C. Geiger, Director of Public Health, San Francisco; Dr. K. F. Meyer, Director, George Williams Hooper Foundation, San Francisco; Dr. Edward Shaw, Director, Contagious Diseases, Childrens Hospital, San Francisco; Dr. Béla Schick, Mount Sinai Hospital, New York, and Miss Margaret Beattie, Associate Professor of Public Health, University of California.

University of California Hospital.

RESULTS OF TREATMENT OF RECURRING CONVULSIVE ATTACKS OF EPILEPSY

HADDOW M. KEITH, M.D.
ROCHESTER, MINN.

WHILE it is true that the therapeutic armamentarium for recurring convulsions (epilepsy) is better than it was before 1900, the principles of treatment have not changed much in the last few decades. Whereas from 1853 to 1912 bromide was the chief anticonvulsant drug, the relatively effective and nontoxic phenobarbital, introduced in 1912, a near relative "mebaral" (n-methylethylphenylbarbituric acid), and the even newer drug diphenylhydantoin sodium U. S. P. ("dilantin sodium") are now available. There are, of course, many other drugs that have been tried, but most physicians rely on these alone or in combination to control epileptic attacks.

In addition to drugs, the ketogenic diet [1] has proved an effective method of treating children who have epileptiform convulsions.

Treatment of such children is especially important. Lennox,[1a] of Harvard Medical School, stated before a subcommittee of the Congress of the United States on May 24, 1945:

> Because epilepsy is predominantly a disease of youth, its prevention and cure, from the economic point of view, is much more important than other diseases, like cancer, kidney and heart trouble, which are primarily diseases of the aged.

In occasional cases, surgical treatment of focal lesions has been an effective method, either alone or in combination with the administration of drugs.[2] It is my purpose, however, to review the relative value of the various methods of treatment other than the surgical procedures. One of the difficulties in judging the value of a treatment is the problem of following the progress of the patients over a number of years and under various conditions. Two groups of patients were selected for

---

From the Section on Pediatrics, the Mayo Clinic.

1. Helmholz, H. F., and Goldstein, M.: Results of Fifteen Years' Experience with the Ketogenic Diet in the Treatment of Epilepsy in Children, Am. J. Psychiat. **94**:1205-1212 (March) 1938.

1a. Lennox, W. G.: Aid to Physically Handicapped: II. Epilepsy, Hearings Before the Committee on Labor, Subcommittee on Aid to Physically Handicapped, House of Representatives, May 24 and 25, 1945, Seventy-Ninth Congress, First Session, p. 1313, Washington, D. C., Government Printing Office, 1945.

2. Penfield, W.: Epilepsy and Surgical Therapy, Arch. Neurol. & Psychiat. **36**:449-484 (Sept.) 1936.

the present study. The first group consisted of consecutive patients observed for from four to five years; the second, of patients given ketogenic diet and followed from four to twenty-two years.

I classified the results of treatment in the following way: 1. Patients who had had no attacks of any kind, so far as was known, for a period of at least one year or for the whole time they had been followed were considered well. 2. Patients whose condition was distinctly better for a few months or a few years were classified as improved. The attacks of these patients had become less frequent or less severe or both, but attacks still occurred. Patients who had had only one or a few attacks in a year were included in this group. 3. Patients who had had no demonstrably favorable effect from the treatment and gave it up were listed as receiving no benefit.

PATIENTS ENCOUNTERED IN 1940 AND 1941

The first group of children in this study consisted of 300 consecutively admitted patients with epilepsy who were examined at the Mayo Clinic in 1940 or 1941 and for whom treatment was started at the time of the examination. On 113 of these patients no follow-up data were available. The remaining 187 patients had continued with treatment and had reported from time to time until 1945. All these patients had grand mal or petit mal or both, and all were treated with diphenylhydantoin sodium and phenobarbital, alone or in combination, with the ketogenic diet or with a combination of the ketogenic diet and the drugs.

Thirty-eight of the 187 patients had gross neurologic lesions, cerebral palsy, mental retardation (including microcephaly) or other gross pathologic processes, such as hemiplegia. The results of treatment of these 38 patients were considered separately. One of the children was free from attacks for at least six months at the onset, and he was the only one who did not receive any treatment. Seventeen (44.7 per cent) were improved so far as their attacks were concerned, and 20 (52.6 per cent) had no effect from treatment. Of the 17 whose condition improved, 8 were treated with phenobarbital; 4, with diphenylhydantoin sodium; 3, with diphenylhydantoin sodium and phenobarbital; 1, with the ketogenic diet alone, and 1, with the ketogenic diet and the drugs. Two patients in this group died while under treatment, 1 of dementia paralytica and the other of hydrocephalus.

There were, then, 149 patients who had no gross handicap but the convulsions and who were followed for four or five years (table 1). Some patients were treated first by one method, then by another.

Thirty-seven patients received the ketogenic diet only. Of these, 10 (27 per cent) remained entirely free from attacks and the condition of 16 (43.2 per cent) improved. A group of 15 patients received the ketogenic diet together with the drugs. Four (26.7 per cent) remained

well. The ketogenic diet was maintained until the patient had beeen free of attacks for one year or more; then it was gradually changed to a normal diet, usually with a moderately limited amount of carbohydrate. When drugs were used in addition to the diet, they were usually continued after the change in diet had been made.

Forty-eight patients received phenobarbital alone. Of these, 6 (12.5 per cent) remained free from attacks, but continued to take full doses of the drug. Thirty-one (64.6 per cent) improved for periods varying from a few months to four years. I have probably erred on the side of leniency and called "improved" any patient who was definitely better for three months or more.

Fifty patients received diphenylhydantoin sodium alone. Six (12 per cent) remained well (while taking the drug), 19 (38 per cent) showed improvement, and 25 (50 per cent) obtained no help. Of the 50 patients

TABLE 1.—*Results of Treatment of Epilepsy in 149 Patients: A Four to Five Year Follow-Up Study* *

Method of Treatment	Total Number of Patients	Freedom from Attacks		Improvement		No Benefit	
		Number	Per Cent	Number	Per Cent	Number	Per Cent
Ketogenic diet	37	10	27.0	16	43.2	11	29.7
Ketogenic diet and drugs	15	4	26.7	3	20.0	8	53.3
Phenobarbital	48	6	12.5	31	64.6	11	22.9
Diphenylhydantoin sodium	50	6	12.0	19	38.0	25	50.0
Phenobarbital and diphenylhydantoin sodium	26	3	11.5	12	46.2	11	42.3

* Several patients received treatment by first one method and then another.

who received diphenylhydantoin sodium alone, 12 (24 per cent) had toxic reactions. These were the only patients in the whole series who had any evidence of toxemia. Their unfavorable reactions may perhaps be explained by their treatment having been begun in 1940, when diphenylhydantoin sodium was a relatively unfamiliar drug.

A final group, of 26 patients, received both phenobarbital and diphenylhydantoin sodium. Three patients (11.5 per cent) had no attacks while under medication.

It is interesting to note that of the two groups receiving the ketogenic diet, about 27 per cent of the patients were well, that is completely free of attacks, for periods of from one to five years. Of all other groups, approximately 12 per cent were well.

Although there did not seem to be much difference in the relative values of phenobarbital and diphenylhydantoin sodium, the former resulted in a higher percentage of patients reporting improvement, while a number of the patients receiving diphenylhydantoin sodium had toxic reactions.

PATIENTS ENCOUNTERED FROM 1921 TO 1930, INCLUSIVE. TREATED WITH KETOGENIC DIET

The second group to be followed included all the patients started on treatment with the ketogenic diet, alone or with drugs, at the clinic during the period from 1921 to 1930, inclusive. The records were studied up to and including 1945; thus, the periods of observation ranged from fifteen to twenty-five years. This group consisted of 311 patients.

TABLE 2.—*Treatment of Epilepsy with Ketogenic Diet: A Fifteen to Twenty-Five Year Follow-Up Study*

		Results					
		Freedom from Attacks		Improvement		Failure	
Group	Total Eligible	Number	Per Cent	Number	Per Cent	Number	Per Cent
Grand mal	44	18	40.9	11	25.0	15	34.1
Petit mal	63	25	39.7	15	23.8	23	36.5
Grand and petit mal	83	24	28.9	9	10.8	50	60.3
Total	190	67	35.3	35	18.4	88	46.3

TABLE 3.—*Periods of Freedom from Attacks as Reported by Patients on Ketogenic Diets*

Period of Relief, Yr.	Total Patients Free of Attack	Grand Mal	Petit Mal	Grand and Petit Mal
4	1	..	0	1
5	2	1	1	..
6	6	3	1	2
7	3	1	1	1
8	6	2	3	1
9	5	1	2	2
10	2	..	1	1
11	4	..	2	2
12	2	..	1	1
13	1	..	..	1
14	2	..	1	1
15	6	2	2	2
16	6	1	3	2
17	4	3	1	1
18	5	1	2	2
19	6	1	2	3
20	4	2	2	..
21	1	..	..	1
22	1	1	..	..
Total patients	67	18	25	24
Mean period, yr.	13.0	13.0	13.1	13.0

Seventy-three of these patients did not cooperate well enough to find out whether the diet would help them or not; and 48 had gross neurologic lesions, including 1 who had a brain tumor. There were, then, 190 patients who gave the diet a fair trial. Sixty-seven patients (35.3 per cent) remained well while following this treatment and after, for periods of from four to twenty-two years (tables 2 and 3). A few of these have not been heard from in recent years. Some may have a recurrence of attacks, but at least it is known that they were well for the periods stated.

The condition of 35 patients (18.4 per cent) was definitely improved, so much so that they were willing to continue the diet for several years. One patient has continued to use it for nineteen years, although it was suggested that she discontinue it after three years. When asked why she kept it up, she said that she was used to it, that its observance was not difficult and that she had only rare attacks while she was using it. Thus, by means of ketogenic diet the attacks of 53.7 per cent of the patients encountered between 1920 and 1930 with so-called idiopathic epilepsy were influenced favorably, and 35.3 per cent were well for long periods (up to twenty-two years; table 3).

It is interesting to note (table 2) that 18 patients who had grand mal (40.9 per cent), 25 who had petit mal (39.7 per cent) and 24 who had both grand and petit mal (28.9 per cent) were free from attacks. This indicates that patients who had grand mal responded best to the diet; those who had petit mal, nearly as well, and those who had both grand and petit mal, somewhat less favorably.

A somewhat similar relation holds true in the group who showed improvement, although the number of patients with both grand and petit mal was about one quarter of the total. The greatest percentage of failures occurred among the patients who had both grand and petit mal (60.3 per cent), the next highest in the group with petit mal (36.5 per cent) and the smallest in the patients with grand mal (34.1 per cent). I can conclude, then, that patients with grand mal alone are most favorably influenced by the diet, that those with petit mal alone are rather favorably influenced and that those with both grand and petit mal are less definitely benefited.

The lengths of time that the patients remained well are given in table 3. Sixty-six of the 67 patients were well for five years or more, and 33 (approximately half) were well for fifteen years or more. The mean period for all the patients remaining free from attacks was 13.0 years.

COMMENT

It is well known that remissions of epileptic attacks may occur. Turner,[3] in 1903, reported that remissions of two years or longer occurred in 13 of 366 patients (3.5 per cent) of all ages who were treated with bromides. Even before the general use of bromides Hufeland,[4] in 1857, reported cures in 5 per cent, Reynolds [5] in 10 per cent

3. Turner, W. A.: A Statisical Inquiry into the Prognosis and Curability of Epilepsy Based upon the Results of Treatment, Med.-Chir. Tr. Edinburgh **86**:259-289, 1903.

4. Hufeland, cited by Turner.[3]

5. Reynolds, R., cited by Turner.[3]

and Trousseau [6] in 13 per cent of cases. Spratling,[7] in dealing with mentally defective patients with epilepsy at Craig Colony, found a 5 per cent expectancy of cure. Penfield and Erickson [8] mentioned that spontaneous remission occurred in 5 per cent of cases. Wilkins [9] studied 200 epileptic children and found that 23 per cent had had remissions for one year or longer and 19 per cent for two years or longer. Wilkins also reported the result of treatment of 30 patients with the ketogenic diet. He found that 8 (26.6 per cent) remained free from attacks for periods of one and a half to six years. This value corresponds closely to the figures given for the patients in my series who were observed from four to five years and for whom the ketogenic diet was employed.

It is impossible, of course, to say when a patient subject to epileptic attacks is cured. Turner [3] and Reynolds [5] found that after a patient had been free from attacks for more than eight years relapses rarely occurred. In my second group, 49 of the 67 patients who were considered well had been free from attacks for nine years or more (approximately 73.1 per cent of all patients who were classified as well and 25 per cent of the 190 who were treated).

It is interesting to compare my second group of patients with Turner's series, as he used a similar classification. Of Turner's 366 patients treated with bromides, the condition of 86 (23.5 per cent) was arrested or the patients were free from attacks. Of the 190 patients in my second group treated with the ketogenic diet, 67 (35.3 per cent) were well. Turner reported improvement in 28.7 per cent of his cases. Of my second group, 18.4 per cent were improved. No benefit was derived from bromides in 47.8 per cent of Turner's patients, and 46.3 per cent of my group received no benefit. Of the patients in Turner's series whose condition was arrested, 15 (17.4 per cent) were cured (by his criteria). By the same criteria, 49 (73.1 per cent) of the 67 patients in my second group who were free from attacks were cured. All Turner's patients took bromides constantly, while the patients of my series discontinued the ketogenic diet in one to three years as a rule.

It is of interest, and perhaps of value, to point out that 29 children were born to 20 of the patients in my second series. The children's

6. Trousseau, cited by Turner.[3]

7. Spratling, W. P.: Epilepsy and Its Treatment, Philadelphia, W. B. Saunders Company, 1909, p. 522.

8. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localizations: A Study of the Mechanism, Treatment and Prevention of Epileptic Seizures, Springfield, Ill., Charles C Thomas, Publisher, 1941, p. 623.

9. Wilkins, L.: Epilepsy in Childhood: I. A Statistical Study of Clinical Types, J. Pediat. **10**:317-328 (March) 1937; Epilepsy in Childhood: II. The Incidence of Remissions, ibid. **10**:329-340 (March) 1937; Epilepsy in Childhood: III. Results with Ketogenic Diet, ibid. **10**: 341-357 (March) 1937.

ages at the time I last heard from the patients ranged from a few months to twelve years. Not one child had been observed to have had convulsions of any sort.

SUMMARY

A comparison of the results of treatment over a period of four to five years of 149 children who had idiopathic epilepsy shows that use of the ketogenic diet or of the ketogenic diet with drugs is the most satisfactory method. Phenobarbital, diphenylhydantoin sodium or a combination of the two were less effective, to about the same degree.

One hundred and ninety patients treated by means of a ketogenic diet between 1921 and 1930 were studied and followed through 1945. Thirty-five per cent of these patients remained well for periods of from four to twenty-two years. Sixty-six of the 67 patients remained well for five years or longer, and 33 remained well for fifteen years or more. Twenty of these patients married and had 29 children. None of the children have had convulsions of any type.

ETIOLOGY OF MONGOLISM

Epidemiologic and Teratologic Implications

THEODORE H. INGALLS, M.D.
BOSTON

A PREVIOUS study of mongolism showed the condition to originate between the sixth and ninth weeks of fetal life.[1] The evidence to be presented here supports this conclusion. It further indicates that the causative agents related to mongolism are relatively numerous, and that the changes effected by these agents in the placental circulation are limited in number and exert their action on the host (embryo) at about the eighth week of gestation. The proof is both epidemiologic and teratologic. All available data have been summarized in order to compare the inferences derived from the one line of reasoning (epidemiologic) with those derived from the other (teratologic).

EPIDEMIOLOGY

Incidence and Prevalence.—The relative frequency of mongoloid as compared to normal infants at the Boston Lying-in Hospital during the years 1931 to 1944 was determined by Beidleman [2] to be 3.4 per thousand live births. From this sampling of some 14,000 births occurring over a thirteen year period in Massachusetts it may be estimated that about 7,000 mongoloid babies are born each year to mothers in America. The annual incidence approximates that of paralytic poliomyelitis or diabetes mellitus.[3]

It is impossible to determine the prevalence of mongoloid persons in the population at large at a specified time, for death during childhood removes an appreciable but undetermined proportion of those afflicted. Warner [4] reported that approximately half of 125 such infants and children died "while under observation" at the Hospital for Sick Children in Toronto. The average length of this period is not stated, but the

This work was aided by a grant from the Perkins Fund.

From the Department of Epidemiology Harvard School of Public Health and the Department of Pediatrics, Harvard Medical School and The Children's and Infants' Hospitals.

1. Ingalls, T. H.: The Pathogenesis of Mongolism, Am. J. Dis. Child. **73**:279 (March) 1947.
2. Beidleman, B.: Am. J. Ment. Deficiency **50**:35, 1945.
3. Marks, H. H.: New England J. Med. **235**:289, 1946.
4. Warner, E. N.; Canad. M. A. J. **33**:495, 1935.

average age at death was 12.6 months. That there is a sizable mortality even in the first few months of life is suggested by the ages of mongoloid infants coming to necropsy at the Infants' and Children's Hospital from 1920 to 1945. Of 37 babies under 2 years of age approximately one third were less than 2 months of age and over half were less than 6 months. Benda,[5] however, pointed out that with improved health conditions and infant mortality on the decline the number of living persons with mongolism may be expected to increase substantially during the next decade—in the absence of any method of prevention.

Seasonal and Annual Distributions of Mongoloid Births.—No data are available on such features as yearly and seasonal frequencies. How-

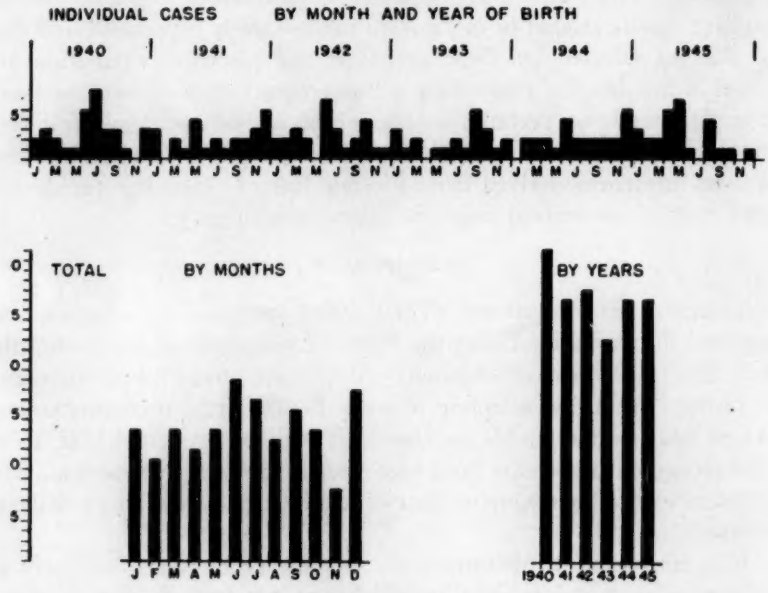

Fig. 1.—Incidence of mongoloid births in Eastern Massachusetts, 1940 to 1945, inclusive.

ever, some information on the frequency with which mongolism occurs in Massachusetts is given in figure 1. This chart is based on the birth dates recorded for those mongoloid patients seen at the Infants' and Children's Hospital, Boston, and the Wrentham State School [6] from January 1940 to September 1946. One hundred and fifty-eight cases arranged by month and year of birth show the occurrence of mongolism during a five year period commencing in January 1940 to have been

5. Benda, C. E.: Mongolism and Cretinism, New York, Grune & Stratton, Inc., 1946.

6. Benda, C. E.: Personal communication to the author.

a relatively regular phenomenon with little tendency to occur in aggregations.

Sex Ratio.—Van der Scheer [7] reported data on 180 males and 136 females, and Brousseau and Brainerd [8] on 184 males and 129 females. From a compilation of four similar series Beidleman [2] arrived at the estimate that 145 mongoloid males were born for every hundred females as compared to the ratio of 105 males to 100 females in the normal population. His totals are not given. The significance of such observations was questioned by Benda and by Brousseau and Brainerd on the grounds that females are more frequently kept at home within the family, while the male is more likely to be committed to an institution.

No common explanation can be brought to bear on the weighting with males of the several small series of mongoloid infants listed in table 1. Beidleman's patients were newborn babies in a lying-in hospital; Comby's experience was in a metropolitan practice or in consultation; likewise the patients brought to the Children's Hospital came for diagnosis or

TABLE 1.—*Mongoloid Infants: Males in Relation to Females*

Series	Males	Females
Beidleman [2]	28	14
Comby, J.: Arch. de med. d. enf. **20**: 505, 1917; ibid. **30**: 5, 1927	50	45
Ingalls	89	59
Twins *	38	32
Multiple cases of mongolism in the same family †	11	7
Total	216	157

* Brousseau and Brainerd.[8] Rosanoff, A. J., and Hendy, L. M.: Am. J. Dis. Child. **48**: 764 (Oct.) 1934.
† Warner.[4] Brousseau and Brainerd.[8]

hoped-for treatment. There is no reason to expect that the cases of mongoloid twins reported in the literature or instances of multiple cases of mongolism in one family should be weighted with males.

The ratio of males to females in this grouping is substantially the same as in the series of van der Scheer and Brousseau. Of the 1,002 mongoloid persons in the three series 580 are males and 422 females.

Relation to Maternal Age.—Bleyer [9] has plotted the ages of 2,822 mothers who gave birth to mongoloid infants against the ages of mothers who produced normal infants during the year 1934. Bleyer's distribution

7. van der Scheer, W. M., in Bonhoeffer, K.: Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten, Berlin, S. Karger, 1927, no. 44.

8. Brousseau, K., and Brainerd, H. G.: Mongolism, Baltimore, Williams & Wilkins Company, 1928.

9. Bleyer, A.: Rôle of Advanced Maternal Age in Causing Mongolism: Study of 2,822 Cases, Am. J. Dis. Child. **55**:79 (Jan.) 1938.

curves (fig. 2) show the peak maternal age in the United States in 1934 to be 24, while the peak age of mothers producing mongoloid offspring was 41.

Likewise in a selected group of primiparas the risk of producing a mongoloid baby was shown to be significantly greater with advancing age.

Order of Birth.—Lahdensuu,[10] Benda, Bleyer and Beidleman have reported data showing that the more children in the family, the more likely the child with mongolism tends to be last. This is consistent with the demonstrated relation of mongolism to advanced maternal age.

Relation of Mongolism to Maternal Ill Health: Hemorrhage and Threatened Abortion.— Schröder [11] reviewed the gestational course of 99 women who gave birth to mongoloid babies, and reported that severe bleeding occurred in 17 (19.5 per cent). Less than 1 per cent

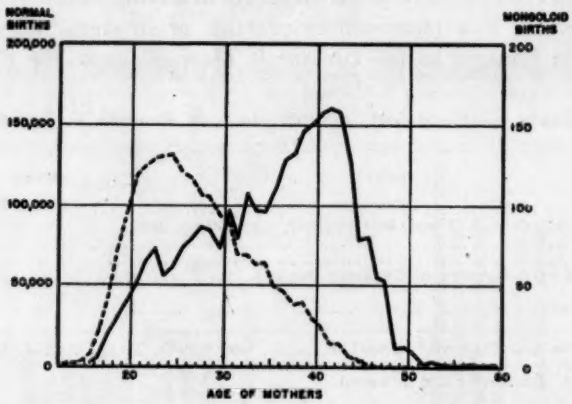

Fig. 2.—Age distribution of mothers of normal (dotted line, United States Registration Area, 1934) and of mongoloid infants (heavy line, total 2,822 collected cases). (After Bleyer.[9])

of 248 mothers of normal babies, comprising a control series, experienced severe gestational bleeding.

Beidleman reported that 9 of 42 (21 per cent) mothers of mongoloid infants delivered at the Boston Lying-in Hospital had hemorrhage during pregnancy.[2] Bleeding in 7 of the 9 occurred during the first trimester at three, one, three, one and a half, two, one and two, and two months respectively (average two months).

Of 75 mothers of mongoloid children surveyed by Benda [5] 24 per cent either attempted abortion or were threatened with spontaneous abortion as evidenced by hemorrhage during pregnancy. Benda, like Schröder, was impressed with the significance of bleeding, as exemplified

10. Lahdensuu, S.: Acta pædiat. **21**:256, 1937.
11. Schröder, H.: Ztschr. f. d. ges. Neurol. u. Psychiat. **163**:390, 1938.

by such statements as the following: "At second month had a large hemorrhage and loss of blood. It was thought to be a miscarriage"; "Was threatened with abortion, had menstrual hemorrhages at second and third month," and, "At time of pregnancy when third menstruation was due had severe hemorrhages lasting five days. Stayed in bed for two weeks." Nine of the 11 patients had bleeding during the first trimester at two, three, three, two and three, two and one-half, one and two, two and three, three, and two months (average two and one-fourth months). For the 7 patients who attempted abortion, the time remains indefinite. One took ergot, another "injections which resulted in a short hemorrhage," and the rest "pills" of unknown composition.

The most striking instance of gestational hemorrhage in the records of the Children's Hospital is that of a mother who gave birth to twins, both mongoloid, on Dec. 30, 1940. She was told that they had separate placentas.[12] At the time of conception she was 36 years of age, "strong and well," and had three children aged 8, 4, and 2½ years. She remembers clearly that the date the twins were due was Jan. 15, 1941. By the obstetric formula of "count back three months and add seven days," it is evident that her obstetrician counted on April 8 as representing her last menstrual period. The probable date of conception, therefore, was around April 22, 1940. She wrote that on June 24, 1940 (approximately sixty days after conception) she was "driving up a mountain road at an approximate speed of 35 miles (56.3 kilometers) per hour. Going around a curve we collided with a car coming down the mountain. The shock was so hard that the steering apparatus was driven down through the boards. My body took the impact as I sat in the seat. . . . I was not unconscious but was shaken up enough to go to bed and stay there, when I got home about two hours after the accident. I don't remember that the hemorrhage awakened me but when I saw the stain it was not bright. A good-sized grapefruit cut in half would have covered it. There may have been a little more in the course of the night, I do not recall. The doctors felt I should stay in bed, which I did for nearly a week."

Acute Intercurrent Infection During Pregnancy.—Ingalls and Davies [13] have recently reported 7 instances of acute intercurrent infections observed during pregnancies which terminated in the delivery of a mongoloid baby (table 2).

They were able to localize the particular disease in 6 of 7 instances at about the end of the second month of pregnancy. The association of 1 case with rubella in the first trimester of pregnancy is noteworthy

12. This has been taken from Dr. William Berenberg's record of the case.

13. Ingalls, T. H., and Davies, J. A. V.: Mongolism Following Intercurrent Infectious Disease in Pregnancy, New England J. Med. **236**:437 (March 20) 1947.

in view of other known instances and of the demonstrated ability of rubella to cause fetal anomalies.[14]

In 1945 Conte, McCammon and Christie [15] reported 5 patients with congenital defects following maternal rubella during early pregnancy. Following rubella at three months, examination showed 1 of them to have "mongolism and congenital heart disease." No comment was made on the circumstance, though the authors discussed the general mechanism whereby rubella might produce pathologic changes in the fetus—blood-borne toxins, disturbed physiologic processes or invasion across the placental barrier. They concluded that "these associations furnish additional evidence that environmental factors operating for the first time after fertilization of the ovum can cause congenital abnormalities."

A third case of mongolism following rubella in the first trimester of pregnancy was recently brought to my attention by Benda.[6] "The mother gave birth to our patient on Aug. 31, 1943. On Dec. 18, 1942, her older child acquired German measles for which a physician was called. A few days later the mother fell ill too with German measles —which must have been between Christmas and the New Year."

TABLE 2.—*Intercurrent Infections in Pregnancies Resulting in Mongoloid Births*

Age of Mother	Intercurrent Infection	Stage of Pregnancy
25	Influenza	2 months
34	Rubella	2 months
39	Mumps	2 months
About 43	Mastoidectomy	2 months
39	Pleurisy	In 3d month
35	Grip	In 6th month
23	Acute purulent otitis media	2 months

Using tables showing the expectancy of pregnancy in different age groups and the reports of the Massachusetts Department of Public Health, Aycock [16] has estimated that the chances that a mother will contract rubella during pregnancy in an epidemic year in Massachussetts (based on 35,000 cases in 1943) is of the order of 1 in 500. The chance of having the disease in the first trimester is, of course, 1 in 3. The chance of producing a mongoloid child is about 1 in 300.[2] It is evidently unlikely for the observed combination of 3 cases of rubella and mongolism to occur by chance. Assuming every year to be an epidemic year for rubella, about 1,350,000 births would be expected to yield 3 such cases when each of the three factors operated by chance.

14. Gregg, N. M.: M. J. Australia **1**:313, 1945.

15. Conte, W. R.; McCammon, C. S., and Christie, A.: Congenital Defects Following Maternal Rubella, Am. J. Dis. Child. **70**:301 (Nov.-Dec.) 1945.

16. Aycock, W. L.: Personal communication to the author.

The total reported congenital deformities after rubella number less than 500,[17] but include 3 instances of mongolism.

Chronic Disorders During Pregnancy.—Many of the advances in medicine have come from clinical observations and suggestions. They have to be subjected to scientific analysis for the development of proof. Syphilis, malaria, tuberculosis and alcoholism in the mother have not infrequently been associated with the subsequent birth of a mongoloid baby, especially in more remote years.[8] Such associations are still occasionally reported in the contemporary literature,[18] though the value to be placed on them remains wholly indefinite. Benda's observations [5] in regard to maternal disease in connection with mongolism are partially summarized in table 3.

In the records of the Children's Hospital associations of such chronic disorders with the subsequent production of a mongoloid child are also to be encountered, although the nature of the maternal disturbance

TABLE 3.—*Pregnancies Resulting in a Mongoloid Child—After Benda*

Chronic Disorders During Pregnancy	Number of Cases in Seventy-Five Cases	Percentage
Involutional pregnancy	9	12.1
Thyroid deficiencies and goiter	10	13.3
Gynecologic disorders	8	10.6
Gallbladder disease	3	4.0
Cardiorenal disorders	5	6.6
History of asthmatic attacks	2	2.6
Total	37	49.2

cannot be regularly assigned to a single category of disease. For example, in one record it was noted that the mother, aged 36, "was sick during pregnancy." She was reached by telephone and mail in August 1946, and this comment was amplified. One other child, aged 12, was living and well when the mother became pregnant about mid-December 1937. The mother had been a life-long sufferer from "menstrual migraine" and had undergone a cholecystectomy in August 1936 with the hope of relieving this condition. Her monthly migraine continued and shortly after she had become pregnant migraine and morning sickness developed into hyperemesis. From mid-January to mid-February she "couldn't keep anything down at all and was confined to bed and fed nothing but tea and toast." At the start of pregnancy she weighed 115 pounds (52.1 Kg.); in the ninth month, 113 pounds (51.3 Kg.).

17. Cordes, F. C., and Barber, A.: Changes in Lens of Embryo After Rubella: Microscopic Examination of Eight Week Old Embryo, Arch. Ophth. **36**:135 (Aug.) 1946.

18. Masia, A.: Riv. di clin. pediat. **39**:65 (Feb.) 1941; abstracted, Am. J. Dis. Child. **64**:377 (Aug.) 1942.

Whether for purposes of classification such a mother represents a case of "gallbladder disease" (cholecystectomy) or of hyperemesis gravidarum is difficult to decide. She unquestionably suffered from a sustained metabolic disturbance during the first trimester of pregnancy.

Another record notes that the mother was " of low grade intelligence and an alcoholic—has been in reformatory several times—patient an illegitimate child." It is scarcely reasonable to classify this mother as "an alcoholic." An alcoholic, criminal, unmarried woman may not represent optimal soil for an embryo, but the reason might be a series of alcoholic debauches, an inadequate diet incident to alcoholism or poverty, or a secret attempt at abortion.

In a third record no prenatal history was given except that the mother was referred from the Boston Lying-in Hospital. That hospital's record revealed that she was 44 years of age when the patient was born and had had seven previous pregnancies with normal deliveries. The eighth pregnancy resulted in a stillborn baby at three months. Examination of the fetus showed "intimations that the age of the fetus was about 12 weeks or younger at the time of death, which has occurred three weeks or more before delivery." The following year she gave birth to a mongoloid child having had "pink staining at time of period, second month." To classify this patient as an example of "involutional pregnancy" is tantamount to saying that she was 44 years of age, for the age would be the sole basis for the classification. The term "involutional pregnancy" does not, for example, rule out the possibility of gynecologic disorders.

That gynecologic disorders can be found in frequent association with subsequent mongolism has been shown by Schröder.[11] By gynecologic examination he found 26 per cent of 99 mothers of mongoloid babies to have a significant degree of retroflexion or prolapse of the uterus, while only 5.5 per cent of the 248 control mothers had such abnormalities. Pathologic changes, including myoma of the uterus, were encountered more frequently in the older age groups (mongoloid series) and when present corresponded in general with gestational bleeding.

Further studies on the relation of chronic maternal systemic and gynecologic disease to mongolism, with adequate controls, are indicated.

Comment.—Epidemiologic Implications: An association between mongolism and relatively advanced age of the mother is clearly shown in Bleyer's curve, figure 2. This alone gives proof of a maternal factor related to advanced age, operating in causation of the condition. The age span encompassed by Bleyer's curve and the several irregularities and eminences at ages other than 41 demonstrate that additional factors must operate.

Three factors have been shown significant. They are gestational hemorrhage, threatened abortion and disorders of the uterus. Hemorrhage tended to occur at about the time the second period was due. Disorders of the uterus were more frequent with advancing years. A fourth factor interpreted as significant is intercurrent infection at about the second month of gestation. Considerable weight is given to the observation of maternal rubella three times in association with subsequent mongolism. That mongolism sometimes follows maternal rubella contracted about the eighth week of pregnancy is not to be construed as meaning that it does so regularly. The probabilities of congenital anomalies in general have been considered elsewhere.[19]

The salient epidemiologic feature that emerges is the common association of mongolism with uterine or systemic disease, present or operating at about the end of the second month of gestation.

TERATOLOGY

Introduction.—The embryo is securely hidden from direct observation and practically all clinical knowledge of embryonic disease is based on inferences drawn from its late manifestations.

The signal contribution of teratology has been the classification and the dating of the origin of many embryologic disturbances. When evidence of a sudden deviation from normal development is found to have occurred, the deviation can usually be classified but can be characterized no more clearly than an "arrest" at some particular stage of development. It is to be understood that the term "arrest" may represent underdevelopment, overdevelopment or any form of abnormal development. The term has morphologic and chronologic but no etiologic significance.

The recent definitive correlation of maternal rubella with congenital anomalies [20] permits both clinician and teratologist to attach etiologic significance to the term "arrest." In the instance of rubella, the arrests are obviously consequential to a virus infection, though the mechanism of their development remains obscure. The consequences, which include congenital cataracts, malformations of the heart and microcephaly, exemplify Ballantyne's definition [21] of the fundamental principle of teratology when he states that "embryonic pathology means abnormal formation." Experience with this agent alone has demon-

19. (*a*) Aycock, W. L., and Ingalls, T. H.: Am. J. M. Sc. **212**:366, 1946. (*b*) Ober, R. E.; Horton, R. J. M., and Feemster, R. F.: To be published.

20. (*a*) Gregg.[14] (*b*) Swann, C.; Tostevin, A. L.; Mayo, H., and Black, G. H. B.: M. J. Australia **1**:409, 1944.

21. Ballantyne, J. W.: Manual of Antenatal Pathology and Hygiene, Edinburgh, W. Green & Sons, 1904.

strated that a supposedly trivial insult may have a profound effect on the fetus; that the arrests produced are not constant; and that at certain periods of gestation specific tissues of the fetus are more vulnerable to the same agent than at others.[22] With these facts in mind and in order to evaluate the significance of the various arrests which characterize mongolism, table 4 has been prepared.

The Synchronisms of Mongolism.—The anomalies frequently grouped about tracheoesophageal fistula as the primary stigma have been termed by Ipsen "synchronisms." [23] Using the word in the same sense, table 4 shows the approximate frequencies of the several more frequent synchronisms grouped about the constant stigmas of mongolism consisting primarily of microcephaly, brachycephaly and relative dwarfism of the basilar bones and the contiguous glabellum, nasal bones and maxilla.[1]

TABLE 4.—*Mongolism: Synchronisms in Relation to Constant Stigmas*

Cranium:	Brachycephaly	Constant
Eye:	Congenital cataracts and opacities	50%
	Epicanthus	39%
Ear:	Maldevelopment and simply convoluted auricles	Constant
Nose:	Acromicria	Constant
	Absence of one or both nasal bones	50%
Palate:	High arch	37%
	Cleft	1%
Larynx:	Maldeveloped, manifested by hoarseness	Constant
Heart:	Septal defects	69%
	Persistent ostium primum	25%
Hand:	Dwarfed middle phalanx, 5th finger	62%
	Syndactyly or webbing of digits	4%
Anus:	Atresia ani	3%

The data presented in table 4 are based on material reviewed in a previous study of the pathogenesis of mongolism.[1] It was then suggested that in the search for agents etiologically related to mongolism attention be centered on the sixth to ninth weeks of fetal life as the time when anomalies susceptible of embryologic orientation apparently arise. During this period skeletal chondrification nears completion, ossification commences, the nose and palate start development and the cerebral hemispheres commence to expand. The brain stem and basilar portion of the skull begin to push forward, fusion of the auricular tubercles occurs and the cavity which exists in the optic stalk starts to close. Septal compartmentation of the heart is brought to completion. The important consideration is that at some time about the ninth week the monstrous-looking embryo becomes the fetus, a miniature replica of an infant, although development is still far from complete.[21]

22. Swann, Tostevin, Mayo and Black.[20b] Aycock and Ingalls.[19a]
23. Ipsen, J., Jr., and Okkels, H.: Hospitalstid. **75**:1083, 1932.

TABLE 5.—*Physiologic Events Pertinent to Mongolism, Sixth to Ninth Week of Fetal Life* *

Week	Eyes	Ears, Nose and Throat	Palate and Teeth	Heart	Hands	Arms
Sixth	Optic vessel has been invaginated by lens vesicle; lens fibers are evident	Site of external ear barely recognizable; fusion of maxillary processes with median nasal process forms external nares	Frontonasal process pushes downward; labiodental lamina has developed	Septum primum has commenced development; primordium of septum secundum apparent	Limbs have lost budlike appearance; tripartite divisioning definite; hands and feet discernible as such; chondrification of fingers commences	Cloacal fossa appears behind genital tubercle
Seventh	Primordia of eyelids have developed; mesoderm has surrounded lens vesicle to form tunica vasculosa lentis containing hyaloid artery; lens fibers fill two thirds of lens vesicle	First fusions of tubercles to form external ear; patency occurs of epithelial plates separating nasal fossae from primitive cavity	Maxillary and intermaxillary processes commence to form; labiodental lamina differentiates into labial lamina and dental lamina	Septum secundum has developed	Metacarpals are represented by 5 slender cartilages surrounded by a dense perichondrium; the phalanges of the first row, except for the thumb, have cartilaginous cores; at the tip of each finger is a mass of condensed mesenchymal tissues; no joint cavities are present	Development of rectum and anal membrane
Eighth	Tunica vasculosa commences to regress, anterior part to become pupillary membrane; lids not fully formed are growing toward each other; lens fibers and nuclei symmetrically arranged in curves convex to exterior surface	Fusion of more tubercles—conchae easily recognizable; anterior portion of epithelial plate differentiates into primitive lip and premaxillary palate; frontonasal process has become nasal septum; ventricles of larynx appear	Union of premaxillary and palatine processes commences anteriorly; primordia of deciduous teeth evident as discrete condensations in horizontal shelf of dental lamina	Subdivisioning of heart and development of valvular apparatus largely completed	First and second metacarpals and distal phalanx of thumb commence ossification; middle phalanges develop cartilaginous cores, with the middle phalanx of 5th finger last to evolve [27]	Anal membrane seen as bulbous partition between rectum and proctodeum
Ninth	Lids approximate over eyes; basic laminated structure of lens apparent; lens vesicle is solid and its basic structure evident	Upper and posterior concha bent forward to cover antihelix; halves of palate have fused; nasal bones appear	Nasal cavity has been largely partitioned from buccal cavity by hard palate; enamel organs and dental papillae have commenced formation	Ostium primum has been closed by fusion of septum I with the endocardial cushions of the atrial canal; ostium secundum almost closed	All metacarpals and all but middle phalanges show grossly visible centers of ossification [24]	Cloaca no longer partitioned by anal membrane

* The sources of the material in this table are as follows: Dodds, G. S.: The Essentials of Human Embryology, New York, J. Wiley & Sons, 1938; Keibel and Mall [26]; Arey, L. B.: Developmental Anatomy, Philadelphia, W. B. Saunders Company, 1954.

The pertinent physiologic events of these weeks are listed in terms of their morphologic manifestations in table 5. The arrangement according to week of gestation is more or less arbitrary because the process of growth is continuous.

Comment.—Reference to table 5 makes clear the synchronized relation of the specific arrests which characterize mongolism to events occurring in the eighth week of fetal life. For example, the presence of a persistent ostium primum indicates that the septum primum and the endocardial cushions developed adequately until about the seventh week, when they were arrested just short of fusion. Were septal arrest to occur in the sixth week some gross septal anomaly such as cor triloculare would be expected, while after the ninth week a patency of the auricular septum could not arise as a developmental phenomenon.

From a chronologic point of view the observed arrests of the middle phalanx of the fifth finger and those of the nasal bones are of crucial importance. The mystery of their association with mongolism disappears when they are considered as synchronisms. In a study of day to day appearances of new centers of ossification Mall [24] concluded that "the remarkable regularity of the appearance of the bones makes them the best index of the stage and age of the fetus we now possess."

To grasp the full significance of the stunted phalanx, it is necessary to recall that there are two main axial gradients of growth, the anteroposterior and the dorsoventral, and that the anatomic position of the hand (relative to the original limb bud) is the supine position, palm forward, radius and ulna parallel, and fifth finger ventrally.[25] Thus, in accordance with the principle of anterior-posterior growth, the primordium of the limb bud develops anteriorly (cephalically) and gives rise in turn to the posterior segments, the arm, the forearm and, finally, the hand. Once the hand commences to chondrify, its segmental differentiation proceeds both dorsoventrally and anteroposteriorly until there comes a time when the last, most posterior, and ventral cartilaginous segment is due to arise. In the upper extremity, this segment will be the middle phalanx of the fifth finger, for the distal phalanges originate directly in mesenchymal condensations similarly to the so-called membranous bones.[26] This exact stage is represented in the accompanying reconstruction of an embryo 20 mm. in length of about 8 weeks of age (fig. 3). The photograph shows only the right hand as seen from the dorsal side and is reproduced from a study on the development of the limbs by Bardeen and Lewis.[27] All the phalanges except

24. Mall, F. P.: Am. J. Anat. **5**:433, 1905-1906.

25. Weatherford, H. L.: Personal communication to the author.

26. Keibel, F., and Mall, F. P.: Manual of Human Embryology, Philadelphia, J. B. Lippincott Company, 1912.

27. Bardeen, C. R., and Lewis, W. H.: Am. J. Anat. **1**:1, 1901.

the middle phalanx of the fifth finger are distinctly represented. A few days later, the precartilage of the middle phalanx would have been present. A few days earlier, other middle phalanges would have been absent (fig. 4).

The extent of the lag between chondrification and calcification—as evidenced by visible depositions of calcium salts in the cartilage matrix—is unknown. It is perhaps of the order of a week, more or less.[28] The preparations of Mall [24] demonstrate that when calcification does occur, the sequence of the appearance of the different centers conforms

Fig. 3.—Endochondral skeleton, right hand (embryo 20 mm. in length). All the phalanges except the middle phalanx of the fifth finger are distinctly represented. (From Bardeen and Lewis.[27])

to the general principles of anteroposterior and dorsoventral gradients of growth. These sequences are demonstrated in figure 5.

Since the precise time of development of the spheno-occipital epiphysis has not been demonstrated, speculation is permitted on its possible relation to the brachycephaly of mongolism. It is suggested that the spheno-occipital primordium is arising at the same time as that of the

28. Ingalls, T. H.: Endocrinology **29**:710, 1941; unpublished experiments.

nasal bones,[29] and usually (in two thirds of the cases) at the same time as that of the middle phalanx of the fifth finger. It is suggested that development of the spheno-occipital cartilage is permanently arrested by the etiologic agent in the same manner as the primordial cartilage of the fifth finger. Proof of the point must await continued pathologic studies. However, there is reason to believe that the spheno-occipital epiphysis plays a prominent part in the forward development of the face,[1]

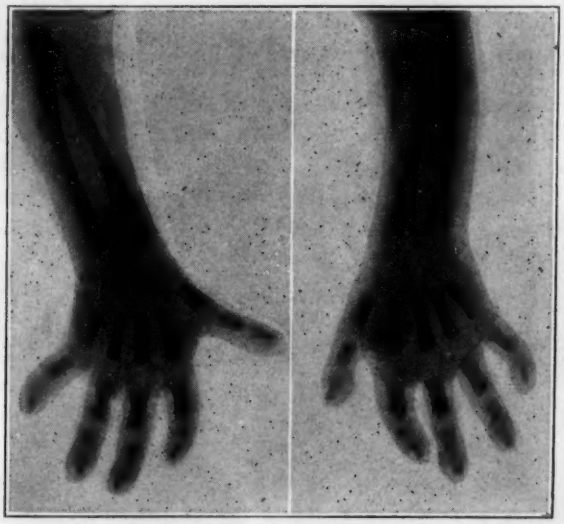

Fig. 4.—Roentgenograms of a mongoloid baby illustrating complete absence of middle phalanges of fifth fingers. Lines of arrested growth in the metacarpals and an arrest of the middle phalanx of the first finger are also discernible. (After Benda.[6])

Fig. 5.—Sequence of appearances of the metacarpal bones and phalanges in the hand of the human fetus. (After Mall.[24])

and the cartilage has been found to show lack of proliferation and regularity [30] and even premature synostosis [31] in mongolism.

---

29. According to Mall, the nasal bones "begin on the first day of the third month and can barely be seen on the 57th day."

30. Benda, C. E.: Am. J. Path. **16**:71, 1940.

31. Greig, D. M.: Edinburgh M. J. **34**:253, 1927.

Sex Ratio.—The trend of available data suggests that mongolism occurs predominantly (about 58 per cent of the time) in males.[32] If verified, this would have a counterpart in certain other congenital conditions such as harelip [33] and pyloric stenosis.[34] Pyloric stenosis was found to affect males in 85 per cent of 1,145 cases reviewed by Ladd, Ware and Pickett.[35]

COMMENT

There is ample teratologic evidence that the times of origin of the arrests which characterize mongolism synchronize at about the eighth week of gestation. There is ample epidemiologic evidence of a significant association between mongolism and maternal disease present or operating at about the same period.

The significance of the association between mongolism and mechanical disorders of the uterus demonstrated by Schröder [11] in approximately a quarter of his patients is open to interpretation. Corner has expressed the opinion [36] that "malposition, deformity or tumors of the uterus give insufficient space for development of the embryo. The usual result if an embryo succeeds in getting itself implanted is expulsion at the second or third month. An embryo developing under such unfavorable conditions with regard to space is likely, as in tubal pregnancy,[37] to become anatomically abnormal because of poor conditions

32. In the first six weeks of gestation the genital primordia show no distinctive sexual differentiation. In the seventh week testicular characteristics are already evident,[26] while those of the ovarian elements do not usually develop until around the tenth week. Development of the gonads and genital primordia, like that of the adrenal cortex is sustained during the sixth to tenth weeks of life, and failure of development (hypergonadism, infantilism and undescended testes) could be interpreted as the result of arrests dating from this period.

33. Warkany, J.; Nelson, R. C., and Schraffenberger, A. B.: Congenital Malformation Induced in Rats by Maternal Nutritional Deficiency: Cleft Palate, Am. J. Dis. Child. **65**:882 (June) 1943.

34. By the seventh week the stomach has reached its permanent position, and its circular muscle layer and pyloric sphincter are indicated by undifferentiated mesenchymal condensations.[26] Differentiation of these two layers is well along by the eighth week, at which time the primordia of the mongoloid anomalies come into being. Pyloric stenosis, however, is occasionally associated with mongolism (Brousseau and Brainerd [8] and Ingalls [1]) and even more frequently with tracheoesophageal fistula (Ipsen and Okkels [23]; Ingalls, T. H.: Unpublished work). An inference is that pyloric stenosis usually originates later than tracheoesophageal fistula (about six weeks) and earlier than mongolism (about eight weeks) but that the time is not sharply demarcated.

35. Ladd, W. E.; Ware, P. F., and Pickett, L. K.: Congenital Hypertrophic Pyloric Stenosis, J. A. M. A. **131**:647 (June 22) 1946.

36. Corner, G. W.: Ourselves Unborn, New Haven, Conn., Yale University Press, 1945, p. 109.

37. Mall, F. P.: J. Morphol. **19**:1, 1908.

which affect its growth." The increasingly frequent association of mechanical disorders and tumors of the uterus with advancing years and parity is common gynecologic experience. Such disorders may represent at least part of the factor related to advanced age which is statistically demonstrable to operate in mothers of mongoloid children.

Another consistent indication of the relation of maternal disease to mongolism is the high incidence (20.4 per cent) of gestational hemorrhages centering at two months among the mothers (216) surveyed by Schröder, Beidleman and Benda. The known relation of hemorrhage to anoxia and the known potentiality of anoxia to damage fetal tissues [38] suggest that anoxia may be an important mechanism in the causation of mongolism. Considerable weight is given to the case of a 36 year old mother who gave birth to mongoloid twins after having been involved in a head-on collision while driving an automobile on the estimated sixtieth day of her pregnancy. The only known result of the accident was body trauma and vaginal hemorrhage. It is inconceivable that trauma of itself could have produced a precisely duplicated disturbance in each of twins, while a placental circulatory mechanism immediately presents itself as the reasonable clinical explanation.

Other than lack of oxygen two other mechanisms with a basis in experimental teratology are the accumulation of toxic metabolites within the fetal circulation and states of dietary deficiency.

Experimental Teratology.—Stockard [39] produced cyclopic fish (Fundulus heteroclitis) embryos by subjecting the eggs in the early stages of development to weak solutions of magnesium chloride. After normal development in sea water had proceeded for periods up to fifteen hours, eggs were placed in magnesium chloride solutions, with the result that many of the embryos showed the cyclopean defect. Shortly after fifteen hours the eggs reach the periblast stage. If then introduced into solutions of magnesium chloride normal two-eyed embryos invariably result. Cyclopia was less frequent when eggs were subjected to solution of magnesium chloride at later stages than when introduced in the solution during the four or eight cell stage.

These experiments demonstrated, first, a vulnerable period for the primordium of the eye at about the time when the optic vesicles are given off from the brain and, secondly, the importance of the action of external or environmental conditions on the developing embryos.

In addition to causing cyclopia, alcohol was shown to exert a much more deleterious effect than magnesium chloride on the ears and central nervous system.[39] After exposure of the embryos at early stages to weak

38. Clifford, S. H.: Am. J. Obst. & Gynec. **39**:388, 1940. Cole, W. C. C.: J. Pediat. **19**:263, 1941.

39. Stockard, C. R.: Am. J. Anat. **10**:369, 1910.

solutions of alcohol the brains developed anomalously with regions of poor differentiation demonstrable in histologic sections. Chlorobutanol, ether and chloroform in weak solutions also inhibited general developmental processes.[39]

These narcotics have since Stockard's time been shown to decrease the oxygen uptake of nerve tissue cells in the Warburg apparatus.[40] The implication that decreased oxygenation of tissue may be a general or local factor in the production of the observed arrests is strengthened by the fact[41] that low oxygen tensions per se may cause anomalous development.[42] McClendon[43] summarized as follows: "A number of monstrosities develop from the eggs of fish, especially those such as trout which require a very high oxygen tension for their development. When the temperature rises and consequently the oxygen tension falls, many abnormal forms appear."

The same general phenomena have been produced in developing chick embryos[44] and in embryonic guinea pigs.[45] Fetal damage has also been brought about in calves as a result of prenatal nutritional deficiencies of the gestating cow.[46] Such skeletal deformities as syndactyly, dwarfism or absence of the tibia or the fibula, and fusion of the ribs have been produced by Warkany and Nelson in the progeny of rats raised on a rachitogenic diet.[47]

Clinical Teratology.—Mall[37] has demonstrated that while only 7 per cent of human uterine pregnancies are productive of a pathologic embryo, 96 per cent of tubal pregnancies so result. He stressed the importance of faulty placentation, such things as partial separation of a normally implanted placenta, or placenta previa, and placentation over a poorly vascularized segment of the uterus related to a myoma or a fibroma. In a survey of 4,446 babies born to mothers with placenta previa[48] the incidence of fetal abnormalities was approximately three times that of cases with a normally implanted placenta.

---

40. Quastel, J. H., and Wheatley, A. H. M.: Proc. Roy. Soc., London, s.B **112**:60, 1932-1933. Jowett, M., and Quastel, J. H.: Biochem. J. **31**:565, 1937.

41. It is also strengthened by Landauer and Bliss's demonstration of anomalous chickens caused by injections of insulin into the embryonating egg (Landauer, W., and Bliss, C. I.: J. Exper. Zool. **102**:1, 1946).

42. Stockard, C. R.: Proc. Am. Philos. Soc. **51**:1, 1912.

43. McClendon, J. F.: Am. J. Physiol. **29**:298, 1911-1912.

44. Stockard, C. R.: Proc. New York Path. Soc. **13**:83, 1913.

45. Stockard, C. R.: An Experimental Study of Racial Degeneration in Mammals Treated with Alcohol, Arch. Int. Med. **10**:369 (Oct.) 1912.

46. Hart, E. B.; McCollum, E. V.; Steenbock, H., and Humphrey, G.: Research Bulletin 17, Wisconsin Agricultural Experiment Station, 1911.

47. Warkany, J., and Nelson, R. C.: Science **92**:383, 1940.

48. Greenhill, J. P.: Am. J. Obst. & Gynec. **37**:624, 1939.

The toxic effect of lead on the human embryo has been established by the observation [49] of 83 abortions or stillbirths among 120 pregnancies in families of lead workers; there were only 37 living births, and 13 of the infants died in the first year of life. Stockard [45] attributed similar ill effect to chronic alcoholism. Aycock and Ingalls [19a] emphasized that rubella in early pregnancy may result in abortion or stillbirth as well as the manifestations known to occur in the living baby,[20] an observation since confirmed by Ober, Horton and Feemster.[19b]

Developments in the field of nutrition suggest that poor nutrition also plays a part in human teratology.[50] Burke, Beal, Kirkwood and Stuart [51] made a nutritional analysis of the diets of 216 women observed throughout pregnancy. The offspring of 31 mothers on a good or excellent diet included 1 baby with an anomalous development of the heart. Congenital anomalies were noted in 8 infants born to 36 women whose diet had been poor or very poor. They included instances of heart disease, cataract, mental retardation, cleft palate and hydrocephalus. One mother had hyperemesis gravidarum during the first trimester of pregnancy.

As a result of long-continued studies Stockard [52] came to the conclusion that two main mechanisms were involved in abnormal development: "In the first case the abnormality may be of germinal origin and . . . hereditary as, for example, albinism, certain legless conditions and polydactyly. These phenomena are not always referred to as monsters, but more commonly as sports. In the second place, true monsters (and the purport of the teratologic data produced here is to stamp mongolism as a monstrous condition) arise from normal ova which have been developed under abnormal conditions or under unusual circumstances." Likewise, Mall concluded [37] that "All monsters are produced by external influences upon normal ova which affect the nutrition of the embryos due to faulty implantation of the ova." The two views are supplementary, rather than contradictory.

Stockard continued:

> The well known congenital defects of the heart and other parts of the vascular system, digestive tract, as well as the numerous developmental arrests in various parts of the body continually remind the observer of the great loss in ability that the race suffers as a result of faulty development. These defects in construction must be considered a disease which causes the death of about 23 per cent of the human race before or shortly after the time of birth, and handicaps a certain proportion

49. Paul, C.: Arch. gén. de méd. **15**:513, 1860; cited by Stockard.[39]

50. Maxwell, J. P., and Miles, L. M.: J. Obst. & Gynaec. Brit. Emp. **32**:433, 1925. Maxwell, J. P.; Hu, C. H., and Turnbull, H. M.: J. Path. & Bact. **35**:419, 1932.

51. Burke, B. S.; Beal, V. A.; Kirkwood, S. B., and Stuart, H. C.: Am. J. Obst. & Gynec. **46**:38, 1943.

52. Stockard, C. R.: Am. J. Obst. **59**:582, 1909.

of the survivors throughout their lives. We carefully study and use all known precautions to protect ourselves against post-natal infections and diseases, and much interest and time is given to combatting the causes, yet little is said and scarcely anything done towards a control of development or the hygienic protection of the developing individual.

These statements were written almost forty years ago. It remained for Gregg, through his studies of rubella, to demonstrate the clinical application of the earlier discoveries of Stockard and Mall. The existing need is for further exploration of the causes of abortions, monstrosities and congenital anomalies through correlated epidemiologic, clinical and teratologic studies.

SUMMARY AND CONCLUSIONS

While the causative agents of mongolism are relatively numerous, the causative mechanisms are few in number and operate at about the eighth week of fetal life. Causative agents include hemorrhage, threatened abortion, pathologic abnormalities of the uterus and certain acute intercurrent infections. Experimental and clinical evidence suggests that lack of oxygen to the fetus may be an important mechanism, with temporary starvation and the accumulation of toxic metabolites to be evaluated.

IMPORTANCE OF BRONCHIAL RUPTURE IN TUBERCULOSIS OF ENDOTHORACIC LYMPH NODES

O. GÖRGÉNYI-GÖTTCHE, M.D.
Head Physician of the St. James Hospital
AND
D. KASSAY, M.D.
Head Physician of the White Cross Hospital
BUDAPEST, HUNGARY

WHEN Kleinschmidt [1] reported, in 1919, that he had observed large shadows in the lungs of tuberculous children and that these shadows disappeared without trace, and when Eliasberg and Neuland,[2] in 1920, stated that these shadows were regressive and harmless—they named them "epituberculous infiltrations"—interest in the "epituberculous infiltration" was stirred up in all parts of the world. It is known that Simon and Redeker [3] found, mostly by roentgen examinations, that these shadows partly around the primary focus and partly around the neighboring lymph nodes represented stored infiltrations. Interest increased when, in 1926, Assmann and Redeker [4] established that the pulmonary tuberculosis of adults also usually begins with infiltrations. These infiltrations are much smaller than the "epituberculous infiltrations"; they are round in shape and mostly located under the clavicle. They were called "early infiltrations" (*Frühinfiltrat*). The whole literature on tuberculosis, especially tuberculosis of children, from 1920 to 1930 was under the influence of these "infiltrations." The main interest in the textbooks of Simon and Redeker [3] and Engel and Pirquet [5] is centered on the description of these "infiltrations." We all studied these new theories with greatest interest. We admit that these clinical and roentgen observations were interesting and beautiful in themselves, but they were lacking in a reliable pathologic base. These infiltrations were of such a mild nature that the majority of the children recovered sooner or later. The fatal cases were caused by various complications.

1. Kleinschmidt, H.: Tuberkulose der Kinder, ed. 2, Leipzig, Johann Ambrosius Barth, 1927.

2. Eliasberg, H., and Neuland, W.: Jahrb. f. Kinderh. **93**:88, 1920.

3. Simon, G., and Redeker, F.: Praktisches Lehrbuch der Kindertuberkulose, ed. 2, Leipzig, Curt Kabitzsch, 1930.

4. Assmann and Redeker, cited by Simon and Redeker.[3]

5. Engel, S., and Pirquet, C.: Handbuch der Kindertuberkulose, Leipzig, Georg Thieme, 1930, vol. 2.

At the end of the thirties some authors, like Jakobaeus,[6] Westermark,[7] Wallgren,[8] Stoloff, Hennel, Korol, Lloyd, Packard,[9] Coryllos[10] and Fleischner,[11] asserted that these regressive shadows derive in large measure from atelectasis, which is caused by the narrowness of the bronchi and which originates from the compression of the tuberculous endothoracic lymph nodes. The further development of this question was greatly influenced by the work of the pathologist Rössle[12] in the year 1936. Rössle[12] compared the roentgenograms made of the living children with the pathologic changes noted at necropsy and found that these roentgenograms were nothing but the roentgenograms of atelectasis. Rössle[12] found that the cause of atelectasis was in most cases the compression of enlarged tuberculous mediastinal lymph nodes, though it happened sometimes that less extensive atelectasis was the consequence of the compression of a primary focus. Rössle[12] distinguished two types of atelectasis: (1) the clear form, which is always mild and occurs as a result of the compression of the enlarged tuberculous lymph nodes, and (2) the obscure form, when the caseous lymph node penetrates into the lumen of the bronchus and obstructs it from inside. The prognosis of the latter form is not favorable, because this form can lead to the development of caseous pneumonia, cavity and bronchogenic spread.

According to Rössle,[12] in the cases of atelectasis in childhood, i. e., in cases of primary tuberculous infection, the clear form is the rule, whereas the obscure form is the exception. Therefore the prognosis of "epituberculosis" in most cases is fair because the atelectasis appears in almost all cases in its "clear form."

In the perspective of the past ten years we must state today that Rössle's[12] work was of fundamental importance and really indicated a turning point in the problem of "epituberculosis" because he showed clearly and exactly the pathologic base of these roentgen shadows which hitherto had been a mystery for medical research.

In later works—R. W. Müller,[13] de Bruin,[14] Alexander and Hasselbach[15] and Düggeli[16]—the influence of Rössle's[12] assertions is

6. Jacobaeus, H. C.: Med. Klin. **28**:673, 1932.
7. Westermark, N.: Med. Klin. **28**:675, 1932.
8. Wallgren, S.: Monatschr. f. Kinderh. **80**:56, 1932.
9. Stoloff, Hennel, Korol, Lloyd and Packard, cited by Düggeli.[16]
10. Coryllos: Beitr. z. Klin. d. Tuberk. **85**:310, 1934.
11. Fleischner, F.: Beitr. z. Klin. d. Tuberk. **85**:313, 1934.
12. Rössle, R.: Virchows Arch. f. path. Anat. **296**:535, 1936.
13. Müller, R. W.: Beitr. z. Klin. d. Tuberk. **91**:273, 1938.
14. de Bruin, cited by Müller.[13]
15. Alexander, H., and Hasselbach, F.: Ztschr. f. Tuberk. **77**:1, 1937.
16. Düggeli: Beitr. z. Klin. d. Tuberk. **97**:108, 1942.

undoubtedly apparent, but the reaction soon set in: Simon,[17] Redeker,[18] Bräuning,[19] Viethen [20] and others violently defended their opinion that these roentgen shadows originate from "infiltrations." Though they admitted that some of these roentgen shadows were indeed atelectasis, on the basis of their clinical and roentgenologic investigations they persisted in their opinion that atelectasis has its proper clinical and especially roentgenologic signs and that if they are lacking one has no right to identify every roentgen shadow with atelectasis. The other authors cited maintained, on the contrary, that atelectasis can occur without the classical roentgen signs. These classical roentgen signs are well known: A part of the lung is diminished and shows a "milk glass shadow" on the roentgenogram and mostly has a sharp borderline. The other parts of the lung show compensatory emphysema. During deep inspiration the heart and other mediastinal organs move to the affected side (Holzknecht-Jakobson sign).

Debates developed so far that in the end no one knew whether a roentgen shadow seen was to be identified with "infiltration" or with "atelectasis," for every one knew that the "classical" roentgen signs had failed.

From the beginning we followed the problem with utmost attention, and we came to the conclusion that with present methods we cannot decide whether a roentgen shadow derives from infiltration or atelectasis. Therefore we had to seek new ways to get nearer to the problem. We chose tomography. We shall not lose time speaking about the importance of tomography; we only emphasize that roentgenograms made by means of tomography show the trachea, the main bronchi and even the smaller bronchi better than any method previously used. Systematic use of tomography was made in every case in which the suspicion of atelectasis or bronchial compression arose. A lecture given by us in the medical society at Budapest in 1944 dealt with the results of these investigations. It was impossible to give a literary report on it, partly because of the war and partly on account of the great number of roentgenograms which would have been necessary to illustrate the cases, but with the improvement of conditions we hope to be able to report particularly on this subject.

From 1940 to 1944 we collected 33 cases. Four cases were of bronchial compression and 29 cases were of "infiltration" or atelectasis. Patients who showed the "classical" symptoms of atelectasis were examined first. When we found that the tomographic roentgenograms

17. Simon, G.: Diagnostik und Klinik der Lungentuberkulose des Kindesalters, Stuttgart, Ferdinand Enke, 1940.

18. Redeker, F.: Ztschr. f. Tuberk. **84**:170, 1940.

19. Bräuning, cited by Redeker.[18]

20. Viethen, A.: Monatschr. f. Kinderh. **67**:85, 1936.

showed in all cases a clearly visible stenosis of the bronchi, we began examinations of those patients in whom the classical symptoms of atelectasis were less obvious or were even completely lacking. The result of these examinations was that in most cases (22 of 29) we could exactly prove the narrowing or obstruction of the bronchi. We had to come to the conclusion that these roentgen shadows originated from atelectasis and that Rössle [12] was right when he stated that "epituberculosis" is nothing but the roentgen picture of atelectasis.

It seemed strange to us that in cases of atelectasis the tomograms did not show narrowing of bronchi so much as obstruction of them, for we saw that the lumen of bronchi seemed to disappear and this gave us the impression that at a certain place the bronchus is obstructed. We were curious to know the cause of the obstruction of the bronchi, and therefore we began systematic bronchoscopic examinations in these cases. Here are the results:

REPORT OF CASES

CASE 1.—R. J., a boy 2 years old, was brought to the hospital with the complaint that three days previously he had suddenly become ill with high fever, loss of consciousness and convulsions. His physician made the diagnosis "febrile convulsions," and thus the boy was sent to us. At the examination the child showed increased breathing. The left lung was somewhat resistant to percussion and the breath sounds were practically absent on that side. Roentgen examination showed that the left lung was almost entirely shadowed, the diaphragm stood much higher on the left side than on the right, and the heart and other mediastinal organs were shifted to the left side, and we saw a "naked spinal column" (fig. 1 *A*). During inspiration the heart and the mediastinal organs distinctly moved to the left side (the Holzknecht-Jakobson sign). It was clear that on the left side of the lung there was atelectasis which was caused by the obstruction of the left main bronchus. Since the clinical symptoms appeared suddenly and the fever developed later we suspected aspiration of a foreign body and decided on bronchoscopy.

Bronchoscopy was done with the patient under ether anesthesia. The inside of the left bronchus was filled with yellowish gray masses which were easily removed (fig. 1 *B*). The right main bronchus was entirely intact. At the beginning we did not know the source of these yellowish gray masses, but when the reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive and the histologic examination showed that the material was a necrotic caseous mass which derived from a caseous lymph node, we found that the cause of the bronchial obstruction was the rupture of a caseous lymph node into the left main bronchus.

Three days after bronchoscopy the boy's temperature became normal, the left lung cleared completely and the moving of the mediastinal organs ceased. The roentgenogram made five days after bronchoscopy showed normal conditions (fig. 1 *C*). The child left the hospital in perfect health after a two week stay.

Comment.—Caseous necrotic masses from a tuberculous lymph node ruptured into the left main bronchus and obstructed it, causing atelectasis in the whole left lung. In the obstructed left main bronchus

inflammation began to develop, indicated by the high temperature. After the obstructing masses had been removed the situation became normal. The bronchial rupture happened without any foregoing symptoms, which made us consider the possibility that a foreign body had been aspirated. Immediate bronchoscopy cleared up the situation and gave quick help.

CASE 2.[21]—K. A., a girl 4 years old, had been feverish for a period of three weeks. Six months later she came to the hospital. Roentgen examination made in the period when she was feverish did not show any pathologic changes. It seemed likely that the primary tuberculous infection was manifested at this time and

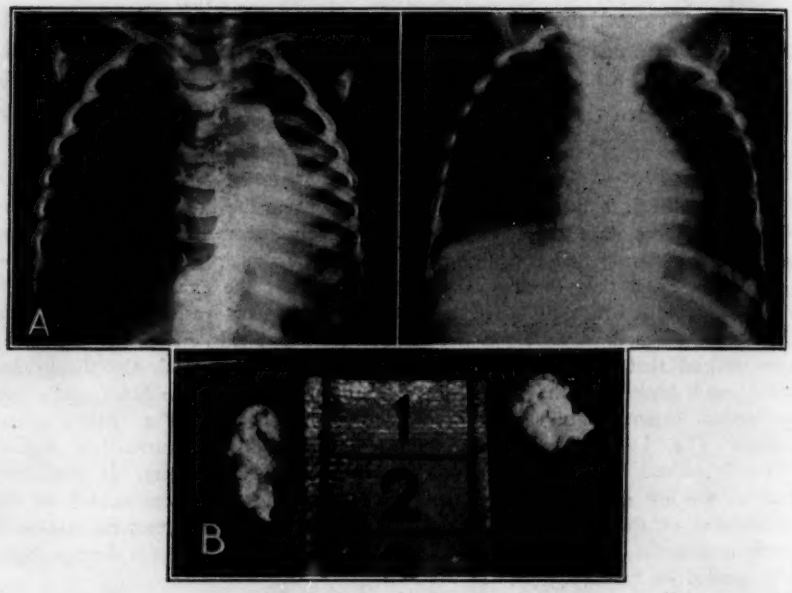

Fig. 1 (case 1).—*A*, atelectasis in the left and compensatory emphysema in the right lung; naked spinal column. *B*, the removed caseous masses. *C*, roentgenogram made five days after bronchoscopy, showing normal conditions.

appeared in the pathologic picture as an "initial fever." The complaint when the child was brought to the hospital was that she had been feverish for two weeks and that she had coughed severely. The physical examination of the chest showed some resistance on the left side, and the breath sounds were less audible on this side. The reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive. The roentgen examination showed atelectasis of the left lung as in the previous case: The left lung, especially in its lower part, was dark, the heart and the mediastinal organs were on the left side and the spinal column was naked. The left side of the diaphragm was high on the right lung, and compensatory emphysema could be seen (fig. 2). At fluoroscopy we could see that during deep inspiration the mediastinal organs moved to the left side; thus the Holzknecht-Jakobson symp-

21. This case was put at our disposition by Dr. A. Szász.

tom was present. Our diagnosis was obstruction of the left main bronchus and atelectasis of the left lung caused by bronchial rupture. The bronchoscopy, made without anesthetic, showed that the right main bronchus was intact, while we could see that in the left main bronchus, 0.5 cm. distant from the bifurcation, the lumen was filled with granulation tissue, which was located mostly on the inner wall of the bronchus. At this time we did not dare to remove this tissue, for we feared that bleeding would set in, and therefore we ceased bronchoscopy.

After bronchoscopy the state of the girl did not show any change, and five days later she was taken home. A year later we saw her again. She had developed well, had no fever and coughed only a little. Physical examinations and roentgenograms showed the same state as a year previously. Bronchoscopy was done again, and the left main bronchus was now totally free. The bronchial rupture was healed, but its sequelae still existed. The fact that the little girl was

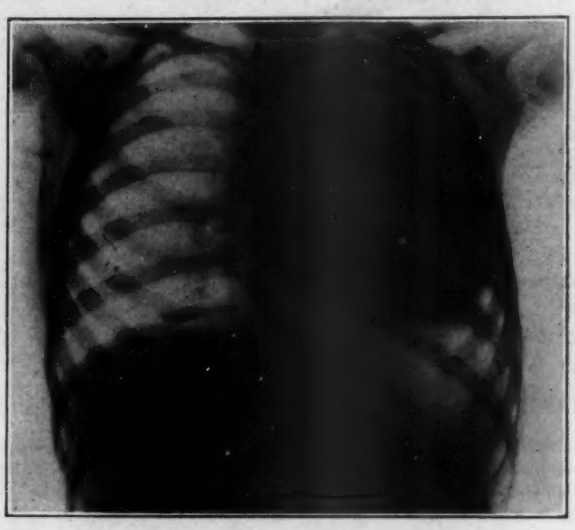

Fig. 2 (case 2).—Atelectasis of the left lung as in the former case.

well in the clinical sense gave us the hope that the sequelae of the bronchial rupture will improve with time.

Comment.—Primary tuberculous infection in a 4 year old girl resulted in stenosis of the left main bronchus six months later and atelectasis of the left lung caused by rupture of a lymph node at the bifurcation into the left main bronchus. This rupture did not pass without leaving its trace, for examination a year later showed that the state of the left lung was the same, although bronchoscopy found the left main bronchus intact. We have no certain proof of what happened in the left lung, but the child's well-being gives us the hope that her health will be restored.

Case 3.—D. P., a girl 3 years old, was brought by her parents; it was stated that a month before a diagnosis of "hilar tuberculosis" had been made. Since that time she had often been feverish and had coughed constantly. The cough had

become severer a week before, and the breath rattling. The girl was well developed and well nourished. The upper side of the right lung gave a little dull sound at percussion and the breath sounds were absent there, while the other parts of the lung were normal. The cough was painful, stenotic, hoarse and sometimes seemed to be of a *toux bitonale* character. Dyspnea was of great intensity and at deep breathing an asthmatoid wheeze was to be heard. The roentgen examination showed that the whole upper lobe of the right lung was darkened with a sharp borderline (fig. 3 *A*). At fluoroscopy the heart and the mediastinal organs moved to the right side; thus the Holzknecht-Jakobson symptom was present. Tomograms were made which showed that the usual shadow of the right main bronchus disappeared soon after the bifurcation (fig. 3), whereas the shadow of the left main bronchus could be seen along its whole course. That, moreover, air could get into the middle and the lower lobe of the right lung was proved by the fact that these parts of the lung showed compensatory emphysema. The tomograms showed that even in the upper lobe of the right lung there were some ectatic bronchi which were filled with air; thus a little air could have come even into them.

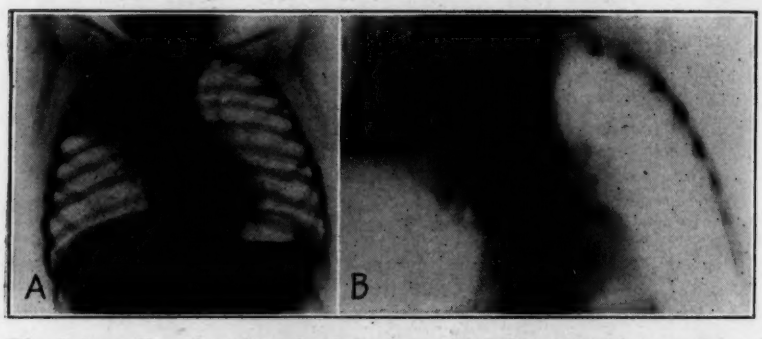

Fig. 3 (case 3).—*A*, atelectasis of the upper lobe of the right lung ending with a sharp borderline. *B*, tomographic roentogram showing that the lumen of the right main bronchus disappears soon after the bifurcation, whereas the lumen of the left main bronchus is visible in its whole course.

The reaction to the Mantoux test (in a dilution of 1 to 10,000) was strongly positive, and the sedimentation rate was 116 mm. after one hour. The child had a high temperature—up to 39 C. (102.2 F.)—even in the hospital, and when her breathing became more and more dyspneic we did a bronchoscopy. Bronchoscopy, performed with the patient under ether anesthesia, showed that the right main bronchus was narrowed and in its beginning was filled with necrotic tissue which could not be removed easily; on account of asphyxia the bronchoscopy had to be interrupted. Even in this case a bronchial rupture occurred, but as we were not sufficiently experienced at this time, we did not dare to remove the necrotic tissue radically. The child's condition after the bronchscopy remained the same for a week; fever ceased, the cough got easier and the asthmatoid wheeze disappeared. The clinical and roentgenologic state of the lung remained the same. The child was taken home six weeks later in this condition.

Comment.—After a month of severe cough which steadily increased dyspnea developed with asthmatoid wheeze in a 3 year old girl. At the same time atelectasis developed with asthmatoid wheeze in the upper

lobe of the right lung and stenosis of the right main bronchus. Bronchoscopy showed bronchial rupture, and the whole right main bronchus was filled with necrotic masses. Bronchoscopy could be done merely for the diagnosis. The child's condition improved by itself, independent of bronchoscopy.

CASE 4.—The patient was D. P., a boy 21 months old. His mother became ill in January 1945, during the battle in Budapest. Correct diagnosis was made only in September, when the roentgen examination showed that the mother's right lung was affected and that a cavity had developed. She was later treated with pneumothorax. After the diagnosis had been made for the mother the child was sent to us to make sure whether he had been infected with tuberculosis

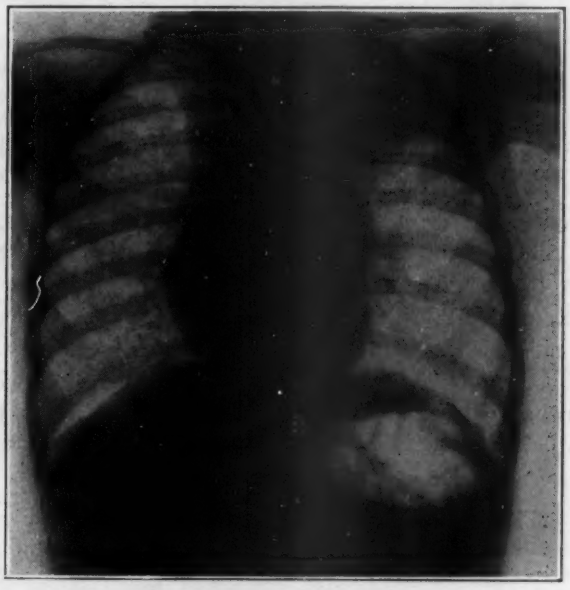

Fig. 4 (case 4).—The trachea shows a great convexity to the right side. The mediastinal shadow is enlarged on the right side and shows "chimney figure." Atelectasis is seen in the upper lobe of the left lung with a sharp borderline and compensatory emphysema, in the lower lobe of the left lung.

from his mother. The child had coughed severely for a month and often had fever and difficulty in breathing. He was taken into the hospital. The breathing became more and more difficult, and later the child showed an asthmatic state. The reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive, and the sedimentation rate was low, between 28 and 30 mm. (The determination of the sedimentation rate was repeated weekly.) Percussion did not show pathologic changes, but at auscultation the breath sounds were not audible on the left side. The roentgenogram showed that the trachea had a great convexity to the right side, and that the upper lobe of the left lung was uniformly shadowed, with a sharp borderline, while the mediastinum was larger on the right side than usual and showed the so-called chimney figure. The lower lobe of the left lung showed pronounced compensatory emphysema (fig. 4). During inspiration the

heart and the mediastinal organs moved to the left side (the Holzknecht-Jakobson sign). According to the results of clinical and roentgen examinations the diagnosis was stenosis of the left main bronchus with atelectasis of the upper lobe of the left lung.

Bronchoscopy was done without any anesthetic, while the child was awake. As the roentgenogram showed, the trachea was out of position to the right side from its middle part downward. We found pale red material the size of a lentil on the lateral wall of the trachea above the entrance of the right main bronchus; we could easily remove it with pincers; otherwise the right main bronchus did not show any pathologic changes. We could not see into the left main bronchus on account of extensive crooking of the trachea. The histologic examination of the removed material (Pathologic Institute of the University of Budapest) revealed necrotic tissue with fibroblasts, epithelioid cells and gigantic cells of the Langhans type. The histologic diagnosis was tuberculosis.

The child was kept under observation for seven weeks. His state improved a little, but a severe cough with asthmatoid attacks set in afresh, though the cough was not so violent as before the bronchoscopy. A year later we saw the child again; he had developed excellently and had not coughed for a long time. Roentgen examination showed that the atelectasis of the upper lobe of the left lung had cleared up, and this time the Holzknecht-Jakobson sign was not present.

Comment.—A boy 21 months old became infected from his mother with the clinical symptoms of bronchostenosis. There developed an obstruction of the left main bronchus with atelectasis of the upper lobe of the left lung. At bronchoscopy, a bronchial rupture was noted on the right side of the trachea above the entrance of the right main bronchus. On account of the great convexity of the trachea the left main bronchus could not be examined. The removal of the necrotic granulation tissue could bring only a little improvement to the child. In this case a double bronchial rupture was present.

Case 5.—B. L., a boy 4 years old, during the battle of Budapest spent six weeks with his parents in a cellar with two hundred persons. There he probably got his primary tuberculous infection. Six months later the child began to cough. A Mantoux test done at this time (in a dilution of 1 to 10,000) brought a positive result and the roentgen examination showed enlarged hilar shadows in both hilar regions. The child was put into a hospital, where he stayed for three months. During this time his condition did not improve, and the cough became more and more severe in the last weeks, while the breathing became difficult. The child was brought to our hospital in the condition described. In our ward the child was constantly feverless, but the sedimentation rate was rather high, between 50 and 60 mm. (weekly determinations were made). Neither percussion nor auscultation revealed any pathologic changes. Breathing was heavy and fast, the cough had a metallic clang, and at the end an asthmatoid wheeze was to be heard. Roentgen examination showed that the upper lobe of the left lung was covered with a non-homogenic spotty shadow. The upper lobe of the right lung was shadowed, too, but its intensity was much less, and the shadow ended with a sharp borderline. In the middle and the lower lobe of the right lung compensatory emphysema was to be seen (fig. 5*A*). The lower lobe of the left lung showed compensatory emphysema, too, which was remarkable only in the frontal direction. During inspiration the heart and mediastinal organs did not show any movement. In roentgen examinations we found more marked atelectasis in the upper lobe

of the left lung, while atelectasis of the upper lobe of the right lung was not so strongly expressed. The character of the cough and the difficulty in breathing made us believe that bronchial rupture would follow, and therefore we performed bronchoscopy.

The child received 2 Gm. of chloral hydrate a half an hour before the bronchoscopy; it fell asleep when bronchoscopy began. The left main bronchus was free, while in the medial wall of the right main bronchus, 0.5 cm. beneath the bifurcation, a grayish white mass was to be seen which was loosely hung together with the wall of the bronchus and was easily removed partly by suction and partly by the child's coughing. The whole caseous mass was the size of a bean

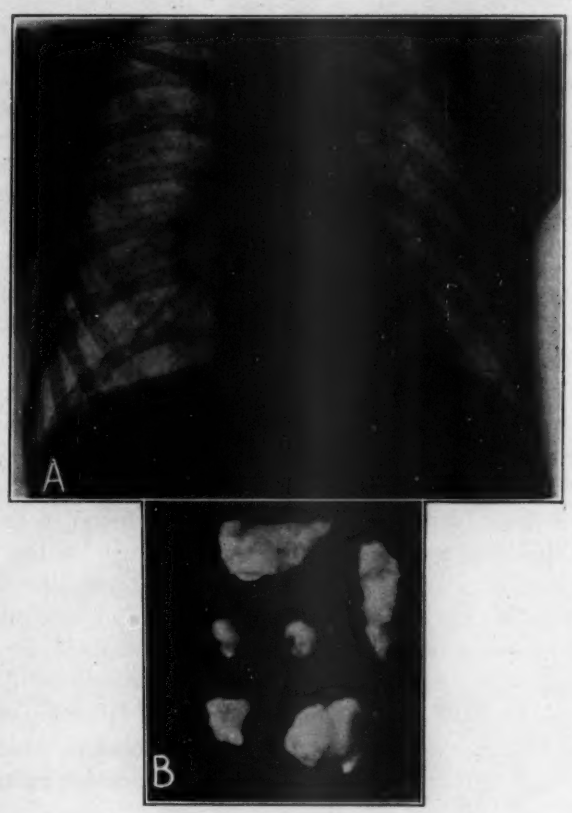

Fig. 5 (case 5).—*A*, the upper lobe of the left lung is covered with a non-homogenic spotty shadow (atelectasis). The upper lobe of the right lung shows a homogenic shadow with sharp borderline (atelectasis also). There is compensatory emphysema in the lower part of the right lung. *B*, removed material.

(fig. 5*B*). The right main bronchus became free after these masses had been removed, and the smaller bronchi became easily visible, too. Histologic examination (Pathologic Institute of the University of Budapest) proved that the caseous mass was of tuberculous origin. After removal of these masses cough ceased and the breathing lost its stenotic character. The child left the hospital after five weeks in a much better condition than before the bronchoscopy.

He was brought back to us five months later. The complaint was that for some weeks there had been difficulty in breathing, the cough had become more severe,

and the child was afflicted with attacks of dyspnea. Otherwise the child's condition was good, and he had no fever. Physical examination did not disclose remarkable changes except some moist rales which were to be heard everywhere. Roentgen examination showed that the shadow of the upper lobe of the left lung was the same as five months before, but the shadow of the upper lobe of the right lung had cleared up completely in consequence of the removal of the caseous mass from the right main bronchus. During deep inspiration heart and mediastinal organs wandered to the left side (the Holzknecht-Jakobson sign). It is remarkable that five months before this sign had not been present, probably on account of bronchostenosis in both lungs, so that the mediastinal organs could not move in either direction. Now, stenosis of the right main bronchus disappearing, the mediastinal organs shifted to the left side because of the continued stenosis on the left side. Bronchoscopy was done again. We found the mucous membrane of the left main bronchus extremely red, and a mass of pus was to be seen around the deviation of the upper and the lower lobe of the left lung; this was removed with suction. Bronchial rupture was not found. The right main bronchus was completely clear. After bronchoscopy the child's condition improved essentially; breathing became normal, though the roentgen shadow of the left main bronchus remained, while the Holzknecht-Jakobson sign disappeared. The child was dismissed in an improved state of health.

Comment.—Atelectasis developed in the upper lobes of the right and the left lung of a 4 year old boy, six months after his primary tuberculous infection. At the first bronchoscopy we found granulation tissue the size of a lentil, which proved that here a lymph node at the bifurcation had broken into the right main bronchus, for this granulation tissue was located in the inner wall of the right main bronchus. Thereby the stenosis of the right main bronchus was solved. At the same time there were no changes to be found in the left main bronchus; therefore we thought that the atelectasis of the upper lobe of the left lung was caused by a perforation into a smaller bronchus of the lobe. Again difficulties in breathing developed five months later. A second bronchoscopy showed that the right main bronchus had become totally clear while the left main bronchus was filled with thick mucous pus. Probably the pus poured from the bronchus of the upper lobe of the left lung and filled the left main bronchus, making breathing and cough difficult. There was double bronchial rupture in this case, also.

Case 6.—S. J., a boy 8 weeks old, had become feverish when he was 4 to 5 weeks old. At the age of 6 weeks he suddenly had dyspneic attacks, which made his mother think that the infant had received Indian corn from his 3 year old brother and had swallowed it. With this complaint the baby was brought to the hospital. The breathing of the well developed and well nourished infant showed little difficulty, and the percussion over the left lung caused a tympanic sound; at auscultation the breath sounds were weaker over the left lung. Roentgen examination showed that the heart and other mediastinal organs were on the right side, the left lung was conspicuously clear and extended, the left side of the diaphragm was deep and the intercostal spaces were more extended on the left than on the right side (fig. 6*A*). Considering the fact that at clinical examination

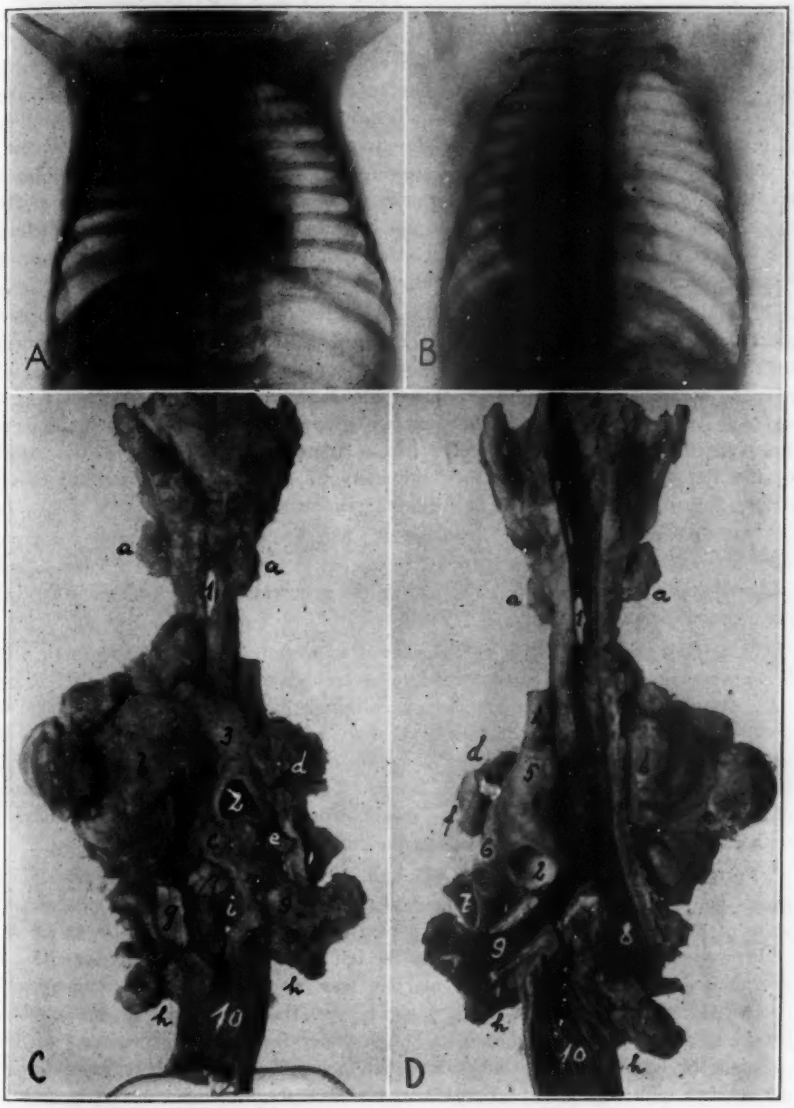

Fig. 6 (case 6).—*A*, obstructive pulmonary emphysema in the left lung. The mediastinal organs are placed to the right side, the left lung is clear and extended, the intercostal spaces are widened, and the diaphragm stands deep. *B*, the obstructive pulmonary emphysema has disappeared in two days after bronchoscopy. *C* and *D*, necropsy specimen (from front and back, respectively); (1) tracheostoma; (2) aorta; (3) arteria anonyma; (4) arteria carotis communis sinistra; (5) arteria subclavia sinistra; (6) ductus botalli; (7) arteria pulmonaris sinistra; (8) right main bronchus; (9) left main bronchus; (10) esophagus; (*a*) lymphoglandula paratracheales; (*b*) lymphoglandula tracheobronchialis dextra; (*c*) lymphoglandula praetrachealis; (*d*) lymphoglandula aortae; (*e*) lymphoglandula epibronchialis; (*f*) lymphoglandula ductus botalli; (*g*) lymphoglandula bifurcationis; (*h*) lymphoglandula bronchopulmonalis. The hairs show the places of perforation into the bronchus and into the esophagus.

over the left lung weaker breath was audible and that the left lung was greatly extended, we suspected obstructive emphysema on the left side, probably caused by aspiration of a foreign body, and an emergency bronchoscopy was done with the patient under ether anesthesia. The tube slipped through the larynx of the 8 week old child without any strain and with an almost insensible jerk. Neither in the right nor in the left main bronchus were any pathologic changes to be seen, except that breathing in the latter was weaker. The cause of the diminished breathing in the left main bronchus remained unknown to us, for the tube of the bronchoscope was too large and could not be put into the bronchus. Nevertheless, the obstructive emphysema on the left side diminished after bronchoscopy, for the mediastinal organs returned almost entirely to their normal place (fig. 6*B*).

The infant's temperature remained high and the difficulty in breathing increased after bronchoscopy. Therefore we performed a tracheotomy with the patient under ether anesthesia. A sharp whistling sound was to be heard before we opened the trachea that indicated that somewhere in the bronchial tubes was a fissure. After tracheotomy and suction two gray pieces the size of a lentil were found in the end of the suction tube. These tissues were, according to the report of the Pathologic Institute of the University of Budapest, of a necrotic tuberculous nature, and tuberculosis bacilli were present.

Now it became clear that the 8 week old baby's difficulty in breathing was not caused by a foreign body in spite of the negative reaction to the Mantoux test (in a dilution of 1 to 10,000); the rupture of a caseous lymph node into the left main bronchus was responsible.

Breathing became a little easier after tracheotomy, but the baby's condition became worse day by day, and on the nineteenth day, during the infant's feeding, milk ran out through the cannula, which indicated that there was a communication between esophagus and bronchus and that an esophagobronchial fistula had developed. Now it was obvious that a lymph node on the left side at the bifurcation had ruptured into the left main bronchus and later into the esophagus, since only lymph nodes at the bifurcation are in contact with the main bronchus and with the esophagus. The baby died on the fifth day.

Postmortem examination (fig. 6*C* and *D*) showed that the caseous lymph nodes had grown together with the left main bronchus and the esophagus and were of the size of a hazelnut, while a part of their necrotic content was missed. A little fissure from this cavity led into the left bronchus. This fissure was 0.5 cm. distant from the bifurcation, its margin was smooth, and the cartilage was destroyed only at the point of the fissure. On the right side, in the tracheobronchial angle, ten entirely caseous lymph nodes the size of a pea were visible. Around the trachea on the left side lymph nodes were similarly caseous though not in such high degree. The lymph nodes around the liver were perfectly normal, which indicated that tuberculous infection had been of extrauterine origin and probably had been acquired just after birth.

Comment.—A 6 week old infant was suddenly afflicted with attacks of dyspnea which gave reason to suppose that a foreign body had been aspirated; in the meantime obstructive emphysema in the left lung developed. Bronchoscopy, done without any difficulty, did not reveal the cause of stenosis. During tracheotomy, performed later, a bronchial rupture was observed. Rupture into the left main bronchus was soon followed by a rupture into the esophagus; thus esophagobronchial

fissure developed which led to death. The bronchial rupture occurred six weeks after the primary tuberculous infection.

CASE 7.—G. M., a girl 8 years old, came to the hospital with the diagnosis of goiter. The child had been coughing for some weeks, the breathing had become somewhat whistling, and the child often tired easily. The reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive. Clinical examination gave no proof of any noteworthy changes in the neck. Percussion of the chest did not disclose any pathologic changes, but a little diminished breathing over the left lung was audible at auscultation. Only enlargement of the hilar shadow on the left side was found at roentgen examination. At deep inspiration the mediastinal organs moved to the left side; thus the Holzknecht-Jakobson sign was present. During expiration the left lung was filled with air, though not in such degree as in the former case. Roentgenograms made during inspiration and expiration (fig. 7) clearly showed that during expiration the left lung contained much more air than the right lung, and the intercostal spaces were also more extended than on the right side, while the left side of the diaphragm became extremely flat. In

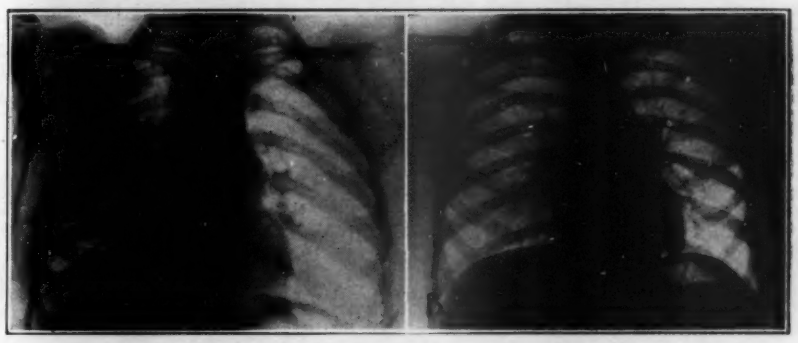

Fig. 7 (case 7).—Obstructive pulmonary emphysema. Roentgenogram made during inspiration (*A*) shows only a little enlargement of the left hilar shadow, while roentgenogram made during expiration (*B*) clearly shows the appearance of emphysema in the left side.

this case we had to deal with distinct obstructive emphysema. The breathing was a little forced, though more or less dyspneic attacks were totally missed, and some whistling was to be heard during expiration. Since the Holzknecht-Jakobson sign and obstructive emphysema on the left side were present, we decided on bronchoscopy, for there was possibility of a bronchial rupture.

The child received 2 Gm. of chloral hydrate, followed later by slight anesthesia with ether before the bronchoscopy. The trachea and the right main bronchus were clear. The left main bronchus was filled 1 cm. from the carina with a pinkish mass with smooth surface which broke up, probably because of the pressure of the tube; the mass was explosively coughed out by the child. The mass was the size of a bean and, according to the histologic report of the Pathologic Institute of the University of Budapest, originated from tuberculous granulation tissue. Fluoroscopy, performed a day after bronchoscopy, revealed that the Holzknecht-Jakobson sign and obstructive emphysema had disappeared. The child's condition is often checked. She is in an excellent state of health, and the fluoroscopic examination shows a normal state.

Comment.—This case differs essentially from the hitherto described cases in that in those cases the symptoms were so "alarming" that every one who had ever occupied himself with the problem of bronchial stenosis knew that somewhere in the main bronchi there must be stenosis, which made an emergency solution necessary. In this case there were no symptoms of pronounced bronchostenosis. The child was brought to the hospital because of fatigue and goiter, and only when asked about coughing did the parents refer to it, while the roentgen examination proved obstructive emphysema. This entirely disappeared after bronchoscopy.

Case 8.—K. K., a boy 3 years of age, became feverish at Christmas 1945. Medical treatment was given. Later otitis media developed. The otitis was treated, but weeks after no improvement was attained the physician suggested treatment

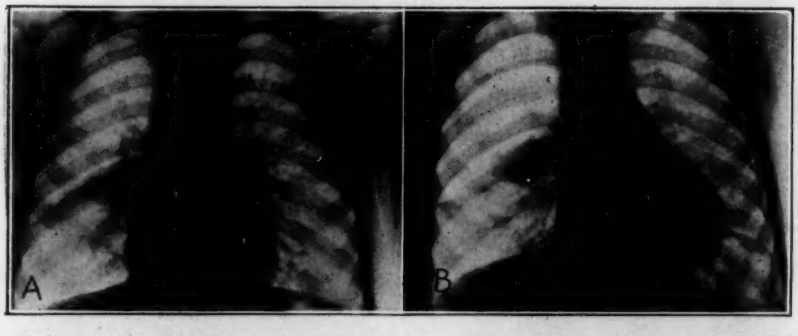

Fig. 8 (case 8).—Obstructive pulmonary emphysema. The roentgenogram made during inspiration (*A*) shows enlargement of the mediastinal shadow and pleuritis interlobaris. At expiration the right lung is widened and the mediastinal organs are shifted to the left side (*B*).

in a hospital. When the child was put into a hospital in Budapest a Mantoux test was given (in a dilution of 1 to 10,000) with positive result. The roentgen examination showed a large mediastinal shadow and an enlargement of the right hilar region; the child was then sent to our hospital. No pathologic changes above the lungs were audible at physical examination. The well developed child was feverless, and the sedimentation rate was 7 mm. Roentgen examination showed that the mediastinal shadow was indeed larger, especially on the right side, with the well known "chimney figure"; a broomlike shadow in the right hilar region was found which was identified as an interlobar shadow in the frontal direction. Mediastinal organs during inspiration shifted to the right side; the Holzknecht-Jakobson sign was present. Moreover, the heart and other mediastinal organs were definitely on the left side during expiration; the right lung remained widened and the right side of the diaphragm flattened. The roentgenograms demonstrate the condition, for they were made during expiration and inspiration (fig. 8). They show that there was obstructive emphysema in the right lung. We believed that there was rupture in the right main bronchus; therefore bronchscopy was carried out.

The child received 1.5 Gm. of chloral hydrate and was brought sleeping into the operating room; bronchoscopy was then performed. The trachea and the left main bronchus were clean, while in the inner wall of the right main bronchus, 0.5 cm. from the carina, granulation tissue was to be found. We removed this tissue with curet and bronchus suction, after which the lumen of the bronchus became entirely free. The histologic report on the removed tissue (of the Pathologic Institute of the University of Budapest) stated that it was tuberculous granulation tissue. Six days after bronchscopy the shifting of the mediastinal organs ceased, and obstructive emphysema disappeared. The child left the hospital in a state of perfect health.

Comment.—Since bronchial stenosis was so slight neither parents nor the physician thought of it. There was no cough at all, and only after long observation and after the roentgen examination did we remark that the breathing was a little difficult. The most reliable symptoms for the diagnosis of bronchostenosis were the Holzknecht-

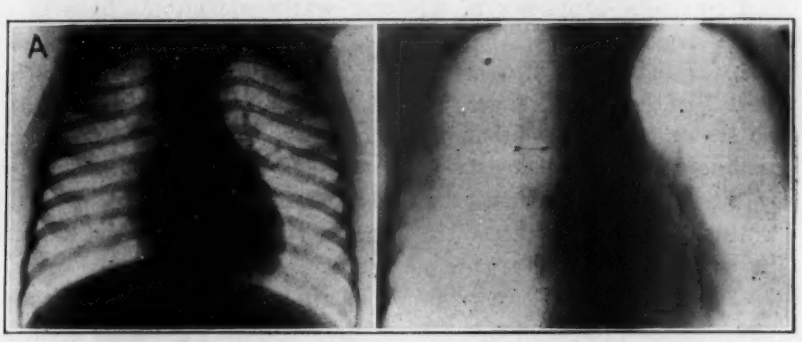

Fig. 9 (case 9).—*A*, widening of the mediastinal shadow on the right side with "chimney figure." No other pathologic changes are visible. *B*, tomographic roentgenograms. On the outer wall of the right main bronchus there is a pea-sized lymph node shadow protruding into the lumen of the right main bronchus.

Jakobson sign and the obstructive emphysema. These two symptoms suggested bronchoscopy, which showed bronchial rupture into the right main bronchus. The child, sent to the hospital with the diagnosis of chronic otitis media, suffered from a bronchial rupture.

Case 9.[21]—D. E., a girl 7 years old, was brought to the hospital by her parents. They complained that during the past three weeks the child had become easily tired and that while hurrying she suffocated and her heart began to beat hard. She was brought to the hospital for an examination of her heart. In the ward the child was feverless, and the physical examination of the lungs did not show any pathologic changes. The reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive, and the sedimentation rate was 20 mm. There was only a little cough. The examination was chiefly directed to the cardiac complaints. No pathologic changes in the heart were to be traced. Roentgen examination showed that the mediastinal shadow had a 1 cm. widening on the right side with "chimney figure" (fig. 9 *A*), while the heart and other mediastinal organs during deep inspiration shifted to the right side. The Holzknecht-Jakobson sign was

present. No other pathologic changes were to be found; neither atelectasis nor obstructive emphysema was present. Tomographic roentgenograms were made. They showed that on the outer wall of the right main bronchus soon after the bifurcation, but still before the branching off of the bronchus of the upper lobe of the right lung, a pea-sized shadow of a lymph node protruded into the lumen of the right main bronchus (fig. 9 *B*).

Roentgen examinations showed clearly that there was a bronchial rupture into the right main bronchus. Bronchoscopy was done with the patient under ether anesthesia. The left main bronchus was free but the right main bronchus showed a gray mass protruding from the outer wall into the lumen at the same place shown by the tomogram. While the tube was introduced this gray mass left its place and was easily sucked out. After suction five to six gray bodies the size of a pea were collected; they were described as caseous tuberculous tissue by the histologic report of the Pathologic Institute of the University of Budapest. When the tuberculous tissue was removed the shifting of the mediastinal organs at once ceased. The child left the hospital in a satisfactory state of health.

Comment.—Diagnosis in this case was made on the basis of the child's complaints of cardiac disease. These complaints were reasonable, for the child when in a hurry breathed more heavily, and her heart beat became stronger, but all these symptoms were caused by the stenosis of the right main bronchus. The only sign of bronchial stenosis was the Holzknecht-Jakobson sign, which was revealed only by the roentgen examination. These cases are to be called cases of "smooth stenosis" because their existence is betrayed only by the moving of the mediastinal organs. As seen in this case, too, the cause of the "smooth stenosis" was a bronchial rupture, for a tracheobronchial lymph node on the right side had ruptured into the right main bronchus. After removal of the tuberculous tissue stenosis ceased, and the child left the hospital in a perfect state of health.

Case 10.—The breathing of F. M., a girl 11 years of age, had become a little difficult during the previous three months, and she had been feverish sometimes. The parents did not remember any other previous diseases or tuberculosis in their family. After the child's admittance into the hospital the sedimentation rate was 18 mm. and the reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive. Physical examination of the lungs did not show any pathologic changes. The child coughed a little, and sometimes during expiration, mostly after considerable moving, a little whistle was to be heard. On the right hand above the fourth metacarpal bone a painless swelling was visible, which roentgen examination disclosed to be tuberculous spina ventosa. Spina ventosa is a product of hematogenic spread that occurs only in a later state of a primary tuberculous infection. Thus we could be sure that the primary tuberculous infection had taken place at least six months before. A compact nut-sized hilar shadow in the left hilar region was found at the roentgen examination. It mostly was covered by the shadow of the heart, but yet it was visible (fig. 10 *A*). By deep inspiration heart and other mediastinal organs were displaced to the left side (Holzknecht-Jakobson sign), showing stenosis of the left main bronchus. Since the other parts of the lungs were perfectly normal, the condition in this case can be called

"smooth stenosis," which was manifested only by the displacement of the mediastinal organs.

Bronchoscopy was carried out with the patient under ethyl chloride and ether anesthesia. After introduction of the tube into the left main bronchus a pea-sized

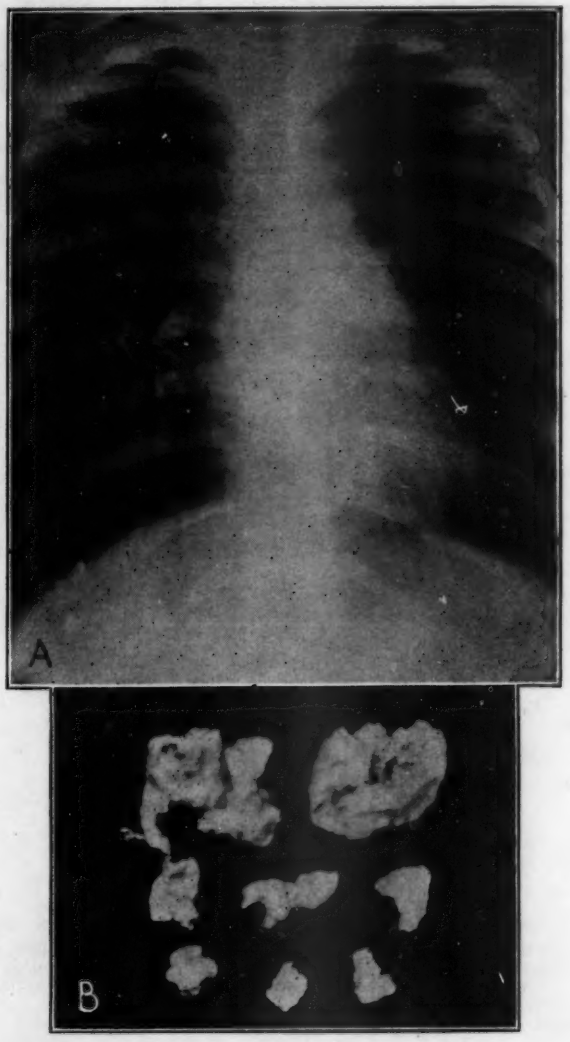

Fig. 10 (case 10).—*A*, here only a compact hilar shadow may be seen which is mostly covered by the shadow of the heart. *B*, caseous masses which emptied into the left main bronchus.

tumor with an undulating surface was found at the bifurication. The tumor seemed to be granulation tissue, and its yellowish contents shone through. After the top of this tissue was grasped with pincers, caseous masses of pea, bean and hazelnut size emptied into the lumen of the left main bronchus. A caseous lymph node was

opened which had been about to perforate. The caseous masses were removed by means of pincers and suction; whereupon the lumen of the bronchus was freed (fig. 10 *B*). The histologic report on the caseous masses was that they were of tuberculous origin (Pathologic Institute of the University of Budapest). The child was discharged perfectly well four days after bronchoscopy. At this time the Holzknecht-Jakobson sign was still present. A control examination two months after bronchoscopy showed the child's health to be good; she did not cough at all. Roentgen examination showed normal conditions, while the Holzknecht-Jakobson sign was entirely absent.

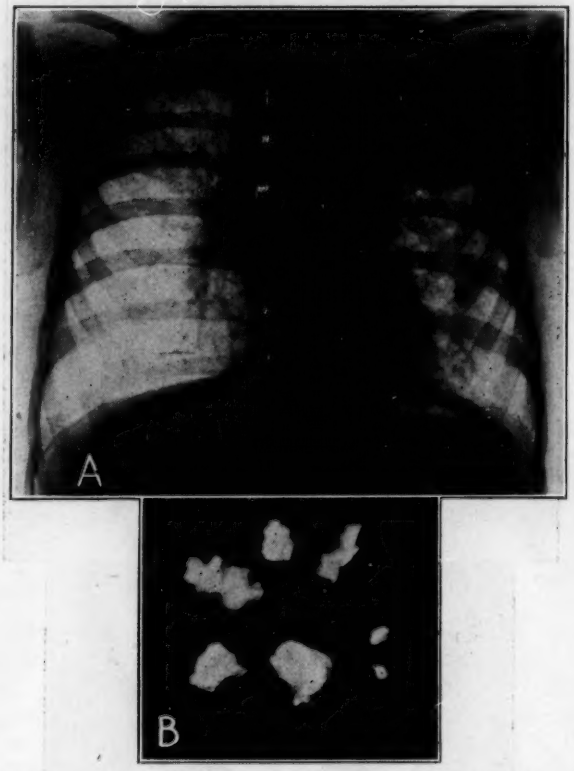

Fig. 11 (case 11).—*A*, the roentgenogram shows only a little enlargement of the right hilar shadow. The child was constantly moving at roentgen examination; therefore the heart seems to be shifted to the left side. *B*, removed caseous masses.

Comment.—The complaints and the clinical symptoms in this case were so insignificant that only by roentgen examination was the stenosis of the left main bronchus discovered through the presence of the Holzknecht-Jakobson sign. During the removal of the granulation tissue a caseous lymph node was opened which was just about to rupture. Many caseous masses came forth which were easily removed.

CASE 11.—H. F., a boy 5 years old, had lived with his grandfather, who died of tuberculosis July 3, 1945. The child began to be feverish in the beginning of

September. A Mantoux test was made (in a dilution of 1 to 10,000) with positive result on September 3. No pathologic changes were shown by roentgen examination. Fever ceased after a few days, and the child's condition was satisfactory. In February, 1946, five months after the primary tuberculous infection, the child began to cough, and even to rattle when moving fast. These were the complaints when the child was brought into the hospital for examination. While in the hospital the child was feverless, lively and mischievous, and his appetite was good. Percussion gave normal results, but a little diminished breathing over the right lung was found at auscultation. During expiration a little asthmatoid wheeze and rattling were sometimes audible. The sedimentation rate was normal, 7 to 12 mm. (weekly determinations were made). Roentgen examination showed only a little enlargement of the right hilar shadow. Since the child moved constantly, one could see on the roentgenogram that the heart seemed to be displaced to the left side (fig. 11). During deep inspiration the mediastinal organs moved to the right side, which indicated that the right main bronchus was narrowed. The Holzknecht-Jakobson sign was present. Because of the weak whistling and rattling and especially because of the Holzknecht-Jakobson sign we suspected bronchostenosis and decided on bronchoscopy.

Before bronchoscopy 2.5 Gm. of chloral hydrate was given to the child orally. The left main bronchus was free, while the right main bronchus was filled with caseous masses the size of a lentil, a pea or a bean. They were removed partly with pincers and partly by coughing. The mass was altogether of hazelnut size (fig. 11 *B*). Histologic examination (made at the Pathologic Institute of the University of Budapest) proved that they were of tuberculous origin. One day after bronchoscopy the moving of the mediastinal organs ceased, and a few days later the child was dismissed in good condition.

Comment.—In this case, also, complaints were insignificant, but here the careful mother remarked that the child was coughing a little, that while he ran his lungs whistled and that when he moved quickly they even rattled. The child gave the impression of being perfectly healthy, and even roentgen examination did not show pathologic changes except the Holzknecht-Jakobson sign. At bronchoscopy the right main bronchus was found to be entirely filled with caseous masses.

Case 12.—S. J., a boy 4 years of age, was brought by his parents into the hospital. The child had been ill six months, had a poor appetite, got easily tired, was feverish and had coughed during the previous weeks. Clinical examination did not reveal any pathologic changes. Reaction to the Mantoux test (in a dilution of 1 to 10,000) was positive, and the sedimentation rate was high (79 mm.). This high rate showed an active process. Roentgen examination showed that the whole upper lobe of the right lung was shadowed by a homogenic shadow with a sharp borderline (fig. 12). During inspiration the mediastinal organs did not show any movement; thus the Holzknecht-Jakobson sign was absent. Neither clinical nor roentgen examination showed signs of bronchial stenosis, but, because the upper lobe of the right lung was atelectatic, we wished to see whether we could find bronchial rupture. We performed bronchoscopy without finding any pathologic changes either in the right or in the left main bronchus. We could not verify our assumption that the atelectasis of the upper lobe of the right lung could

have been caused by the rupture of a caseous lymph node into a smaller bronchus, for it was impossible to look into the bronchus of the upper lobe of the right lung.

The child was kept in our ward because he was almost always feverish. Later fever increased, and one month after bronchoscopy the child had a severe headache, which showed that tuberculous meningitis had developed. Nine days later the child died. Postmortem examination revealed the following data (Pathologic Institute of the University of Budapest): A plum-sized caseous focus was visible in the side of the upper lobe of the right lung. In the middle of the lobe a caseous lymph node was found which had ruptured into the bronchus of this lobe and had partly obstructed it. An atelectatic area of 3 to 4 fingerbreadths extended from the primary focus to the neighborhood of the hilar region. There were some bean-sized caseous lymph nodes in the right hilar region and around the trachea. The brain showed the characteristic changes of tuberculous meningitis, and besides this miliary tuberculosis was to be found everywhere.

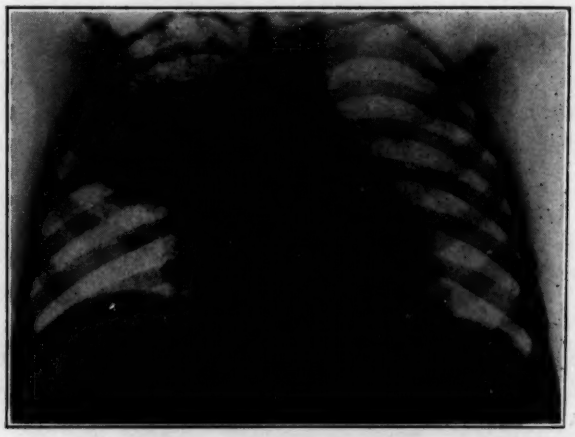

Fig. 12 (case 12).—Atelectasis of the upper lobe of the right lung with a sharp borderline.

Comment.—A homogeneous shadow with a sharp borderline was present in the upper lobe of the right lung. This shadow formerly was called "infiltration." Since there were no signs of bronchostenosis we wished to see whether any traces of bronchial rupture were to be found. Bronchoscopy was done without any result. Tuberculous meningitis which developed a month later caused the death of the child. Post-mortem examination showed that the roentgen shadow represented atelectasis. There was a rupture in the bronchus of the upper lobe of the right lung. This bronchial rupture was not visible at bronchoscopy, because it was situated in the upper lobe of the right lung.

COMMENT

So far bronchoscopy has been carried out in 28 cases; 12 of these were described in particular. The rest will not be described in detail

because they do not show anything new. We thought it more reasonable to collect all cases and put them in a table where all important data are included (table 1).

TABLE 1.—*Data on Cases of Atelectasis in Which Bronchoscopy Was Performed*

Case; Name	Age; Sex	Diagnosis	Place of Bronchial Rupture	Removed Material
1 R. J.	2 yr. M	Atelectasis of left lung; Holzknecht-Jakobson sign	Rupture of an unknown lymph node into left main bronchus	Necrotic, caseous masses
2 K. A.	4 yr. F	Atelectasis of left lung; Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into left main bronchus	
3 D. P.	3 yr. F	Atelectasis of upper lobe, right lung; stenosis of right main bronchus; Holzknecht-Jakobson sign	Rupture of an unknown lymph node into right main bronchus	
4 D. P.	21 mo. M	Atelectasis of upper lobe, left lung; stenosis of left main bronchus; Holzknecht-Jakobson sign	Rupture of tracheobronchial lymph node into right main bronchus; rupture of another, unknown lymph node into bronchus of upper lobe, left lung; double bronchial rupture	Granulation tissue
5 B. L.	4 yr. M	Atelectasis of upper lobe, both lungs; no Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into right main bronchus; rupture of another, unknown lymph node into bronchus of upper lobe, left lung; 5 mo. later thick mucous pus in left main bronchus; double bronchial rupture	Caseous masses; later mucous pus
6 S. I.	8 wk. M	Stenosis of the left main bronchus with obstructive emphysema; later esophagobronchial fistula; no Holzknecht-Jakobson sign; postmortem examination	Rupture of lymph node at bifurcation into left main bronchus and 5 days later into esophagus	Caseous material
7 G. M.	7 yr. F	Stenosis of the left main bronchus with obstructive emphysema; Holzknecht-Jakobson sign	Rupture of unknown lymph node into left main bronchus	Granulation tissue
8 K. K.	3 yr. M	Stenosis of right main bronchus with obstructive emphysema; Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into right main bronchus	Granulation tissue and caseous material
9 D. E.	7 yr. F	Stenosis of right main bronchus; Holzknecht-Jakobson sign	Rupture of tracheobronchial lymph node into right main bronchus	Caseous necrotic tissue
10 F. M.	11 yr. F	Stenosis of left main bronchus; Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into left main bronchus during bronchoscopy	Granulation tissue and caseous masses
11 H. F.	5 yr. M	Stenosis of right main bronchus; Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into right main bronchus	Granulation tissue and caseous masses
12 S. J.	4 yr. M	Atelectasis of upper lobe, right lung; no Holzknecht-Jakobson sign; postmortem examination	Rupture of bronchopulmonary lymph node into secondary bronchus of upper lobe, right lung	
13 P. E.	9 yr. F	Stenosis of left main bronchus with obstructive emphysema; Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into left main bronchus	Granulation tissue and caseous material
14 B. G.	3 yr. M	Atelectasis of upper lobe, right lung; stenosis of right main bronchus; Holzknecht-Jakobson sign	Rupture of tracheobronchial lymph node into right main bronchus	Granulation tissue and caseous material

Of the 28 cases in the table 18 showed bronchial rupture, and 3 showed only an encroaching of the lymph nodes on the lumen of the main bronchus; in 7 bronchoscopy was without result. The latter cases

TABLE 1.—*Data on Cases of Atelectasis in Which Bronchoscopy Was Performed—Continued*

Case; Name	Age; Sex	Diagnosis	Place of Bronchial Rupture	Removed Material
15 K. T.	6 yr. M	Atelectasis of upper lobe, left lung; stenosis of left main bronchus; Holzknecht-Jakobson sign	Rupture of bronchopulmonary lymph node into bronchus of upper lobe, left lung; 2 wk. later purulent sputum	Caseous masses
16 B. J.	2 yr. M	Stenosis of left main bronchus; Holzknecht-Jakobson sign	Rupture of unknown lymph node into left main bronchus	Granulation tissue and caseous material
17 P. S.	5 yr. M	Atelectasis of upper lobe, left lung; stenosis of left main bronchus; Holzknecht-Jakobson sign	Rupture of lymph node at bifurcation into left main bronchus and of unknown lymph node into left main bronchus; double bronchial rupture	Granulation tissue and caseous material
18 L. M.	9 yr. F	Atelectasis of lower lobe, left lung; Holzknecht-Jakobson sign	State after bronchial rupture; purulent mucus in left main bronchus; after suction, recovery within 2 wk.	Purulent mucus
19 B. I.	2 yr. M	Stenosis of left main bronchus; Holzknecht-Jakobson sign	Bronchopulmonary lymph node encroached on left main bronchus	
20 B. I.	11 mo. F	Atelectasis of upper lobe, left lung; no Holzknecht-Jakobson sign	Tracheobronchial lymph node encroached on left main bronchus	
21 S. E.	7 yr. F	Atelectasis of upper lobe, right lung; no Holzknecht-Jakobson sign	Encroaching of lymph node at bifurcation into left main bronchus	
22 I. E.	6 yr. F	Atelectasis of middle lobe, right lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	
23 B. E.	8 yr. M	Atelectasis of middle lobe, right lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	
24 V. C.	18 mo. M	Atelectasis of upper lobe, right lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	
25 N. E.	6 yr. F	Atelectasis of upper lobe, left lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	
26 K. J.	5 yr. F	Atelectasis of lower part of upper lobe, left lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	
27 K. M.	17 mo. F	Atelectasis of lower part of upper lobe, left lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	
28 L. J.	14 mo. M	Atelectasis of part of the middle lobe, right lung; no Holzknecht-Jakobson sign	Bronchoscopy without result	

will be discussed elsewhere. Bronchoscopy in these cases was made entirely because of scientific interest, for all the symptoms of bronchostenosis were lacking.

If cases in which the bronchial rupture was demonstrable are considered, the conclusion is reached that all the different pathologic

pictures, both in the cases in which there were severe attacks of dyspnea (cases 3 and 4) and in cases in which clinical symptoms were almost lacking (cases 7, 8, 9, 10, 11 and 12) have a common cause: the rupture of caseous lymph nodes into the bronchi.

This pathologic picture has long been known by the pathologists and clinicians. The first cases were naturally described mostly by pathologists—for instance, in the book of Rilliet and Barthez [22] in 1843. This book contains 27 cases which were discovered by postmortem examination. These cases were rounded up to 50 by Weil [23] in the year 1878. The clinical symptoms of bronchial stenosis and bronchial rupture are also described by the famous clinician Widerhofer.[24] Oekonomides [25] in 1882 reported the first case in which a child with bronchial rupture survived. This child's life was saved by the fact that it spontaneously coughed out the ruptured caseous masses. Already physicians were performing tracheotomy in cases in which children were suffocating, but then tracheotomy did not bring much success. Saving of a child's life was reported in 1885 by Petersen.[26] Since tracheotomy carried out by Petersen [26] in the case of a suffocating 6 year old girl brought no success, he introduced a Nélaton catheter into the trachea, and thus removed some caseous pieces. The breathing became easier, and more caseous masses were coughed out. The child's life thus was saved. This period was closed by Ebert [27] in his monograph of 1908, in which he described 144 collected cases of bronchial rupture, in only 9 of which (6.2 per cent) was life preserved. The bronchoscope was discovered by Kilian [28] in 1897, and von Eicken [29] and Schrotter [30] used it from 1904 in cases of bronchial rupture. In the diagnosis of bronchial stenosis the discovery of Roentgen was of decisive importance (1896). Holzknecht [31] and Jakobson [32] in 1899 described the most important roentgen signs of bronchial stenosis, the moving

22. Barthez, E., and Rilliet, F.: Traité clinique et pratique des maladies des enfants, Paris, G. Baillière, 1843.

23. Weil, in von Gerhardt, C.: Handbuch der Kinderkrankheiten, Tübingen, H. Laupp, 1878.

24. Widerhofer, W., in von Gerhardt, C.: Handbuch der Kinderkrankheiten, Tübingen, H. Laupp, 1878, vol. 3, pp. 973-1021.

25. Oekonomides, G.: Ueber chronische Bronchialdrüsen-Affectionen und ihre Folgen, Inaug. Dissert., Basel, F. Riehm, 1882.

26. Petersen: Deutsche med. Wchnschr. **10**:145, 1885.

27. Ebert, O.: Ueber den Durchbruchkäsiger Bronchialdrüsen in benachbarte Organe, Inaug. Dissert., Hamburg, L. Voss, 1908.

28. Kilian, cited by Denker, A., and Kahler, O.: Handbuch der Hals-Nasen-Ohrenheilkunde, Berlin, Julius Springer, 1927.

29. von Eicken, C.: Arch. f. Laryng. u. Rhin. **15**:371, 1904.

30. Schrotter, H. V.: Klinik der Bronchoskopie, Jena, Gustav Fischer, 1908.

31. Holzknecht: Wien. klin. Rundschau, **25**:2345, 1899.

32. Jakobson: Deutsche med. Wchnschr. **39**:265, 1913.

of the mediastinal organs to the stenosed side. Roentgen signs of obstructive pulmonary emphysema were described by Arnsberger [33] in 1909 and by Ziegler [34] in 1913.

In spite of the fact that the clinical and roentgen diagnosis and even bronchoscopy of bronchial stenosis and bronchial rupture were perfectly worked out in the beginning of this century, these pathologic pictures penetrated only slowly into general medical knowledge, and even today their acceptance is slow, as is proved by the fact that from the time of Ebert's [27] work up to the present reports have been published in which only 1 or 2 cases of bronchial stenosis or rupture are described; this indicates that their authors believe their cases of sufficient rarity and importance to be reported. We do not ascribe great importance to the collecting of all reported cases; we only mention that H. Koch [35] reported a case in 1911 in which a child suffering from bronchial rupture was saved. Single cases were described by Knöpfelmacher and Pollak [36] and Dinda [37]: in 1912. Hecker [38] and Oeri [39] also reported single cases in 1913. In 1924 a case was reported by Minnigerode and Gottstein [40] in which bronchoscopy was performed with success. A case in which a 4 year old boy coughed out spontaneously ruptured caseous masses was reported by Malmberg [41] in 1932. Eliasberg [42] in 1933 reported 4 cases of obstructive emphysema, and in the same year Orel [43] reported 2 cases, while Morlock and Pinchin [44] reported 1 case with recovery. In 1934, 33 cases in which bronchoscopy was done were reported by Paunz.[45] Fourteen cases were his own, while the rest was collected from the literature. In the same year a case was reported by Scobie.[46] The same author collected almost all the cases of bronchial rupture published in the literature up to 1934. Scobie [46] collected 20 cases with recovery and 74 cases with

33. Arnsberger, H.: Die Röntgenuntersuchung der Brustorgane, Leipzig, F. C. W. Vogel, 1909.

34. Ziegler: Deutsche med. Wchnschr. **39**:2238, 1913.

35. Koch, H.: Wien. med. Wchnschr. **61**:1046, 1911.

36. Knöpfelmacher and Pollak: Ztschr. f. Kinderh. **1**:197, 1912.

37. Dinda: Zentralbl. f. Kinderh. **2**:93, 1912.

38. Hecker: Ztschr. f. Kinderh. **5**:420, 1913.

39. Oeri, F.: München. med. Wchnschr. **60**:410, 1913.

40. Minnigerode, W., and Gottstein, W.: Klin. Wchnschr. **3**:2390, 1924.

41. Malmberg, N.: Acta pædiat. **13**:357, 1932.

42. Eliasberg, H.: Jahrb. f. Kinderh. **139**:12, 1933.

43. Orel, H.: Jahrb. f. Kinderh. **139**:1379, 1933.

44. Morlock, H. V., and Pinchin, A. J. S.: Lancet **1**:1114, 1933.

45. Paunz, M.: Acta oto-laryng. **21**:279, 1934.

46. Scobie, R. B.: Acute Asphyxia from Intrabronchial Rupture of Tuberculous Mediastinal Gland with Recovery, Am. J. Dis. Child. **48**:373 (Aug.) 1934.

fatal outcome. Faust [47] and Dietl [48] each reported 1 case in 1936. Spivek [49] reported 4 cases of obstructive emphysema and collected 18 cases from the literature. In 1938 2 fatal cases were described by Vortmann,[50] and in 1944 a fatal case was reported by Pray.[51]

Though some pathologists, like Huebschmann,[52] stated that bronchial rupture seldom occurs, Ghon [53] stated, in 1910, that of 184 cases of tuberculosis in children in which necropsy was done bronchial rupture was present in 30 (17.7 per cent). Ranke [54] emphasized in 1913 that bronchial rupture appears more often than is commonly believed. De Velasco,[55] at the institute of Loeschke, in 1932, at autopsy of tuberculous children found bronchial rupture among 18.7 per cent. Autopsies done by us in the White Cross Hospital of Budapest during the years 1932 to 1942 revealed 9 cases of bronchial rupture (11.3 per cent) among 79 children who died of tuberculosis.

The clinicians Simon and Redeker [3] in 1930 wrote that "the pathologic picture of bronchial rupture is better known to the pathologists than to the clinicians." They also pointed out that "bronchial rupture is not too frequently present." They described 3 cases of bronchial rupture. Engel [5] in the 1931 edition of the work by Engel and Pirquet wrote that "though bronchial rupture is not too frequent it is not so rare that an experienced clinician should not have opportunity to meet with it periodically." Chevalier Jackson [56] in 1927 wrote: "In a number of instances, the entire lumen of the bronchus was occluded by cheezy débris of a peribronchial gland which had eroded through."

About the frequency of bronchial rupture opinion has changed among the specialists. "Infiltration" laid the basis for the discussion on this question. Lately more and more authors came to the opinion

47. Faust, O. A.: Primary Tuberculosis, Obstructive Pulmonary Emphysema and Asthma with Recovery, Am. J. Dis. Child. **51**:118 (Jan.) 1936.

48. Dietl, K.: Arch. f. Kinderh. **108**:65, 1936.

49. Spivek, M. L.: Obstructive Pulmonary Emphysema Due to Partial Obstruction of the Bronchi by Tuberculosis Lesions, Am. J. Dis. Child. **51**:69 (Jan.) 1936.

50. Vortmann, M.: Kinderärztl. Praxis **9**:49, 1938.

51. Pray: J. Pediat. **25**:253, 1944.

52. Huebschmann, P.: Pathologische Anatomie der Tuberkulose, Berlin, Julius Springer, 1928.

53. Ghon, A.: Der primäre Lungenherd bei der Tuberkulose der Kinder, Vienna, Urban & Schwarzenberg, 1912.

54. Ranke: Ztschr. f. Kinderh. **5**:420, 1913.

55. de Velasco: Beitr. z. Klin. d. Tuberk. **81**:675, 1932.

56. Jackson, C.: Bronchoscopy and Esophagoscopy: A Manual of Peroral Endoscopy and Laryngeal Surgery, ed. 2, Philadelphia, W. B. Saunders Company, 1927.

that these "infiltrations" were nothing but atelectasis. This leads to the question: What is the cause of this atelectasis? R. W. Müller [57] wrote in 1939: "Rupture of caseous lymph nodes into the bronchi occurs not too rarely in childhood and is often the source of open tuberculosis." Hamburger,[58] expert on children's tuberculosis, wrote in 1942: "Bronchial rupture probably occurs more often than was hitherto believed, and there are many benign cases among them, for the lymph node penetrates slowly into the bronchus and the caseous masses can be coughed out by the children."

The incidence of recovery in cases of bronchial rupture was found to be 6.2 per cent by Ebert [27] in 1908 and 20.2 per cent by Scobie [46] in 1934. The pathologists are rather pessimistic about the prognosis. In 1930 Beitzke [59] stated that bronchial ruptures are fatal in almost every case, for even if bronchial rupture does not cause sudden death the ruptured material is spread into the lungs, causing fatal bronchogenic tuberculosis. Beitzke [59] admitted, however, that cases can be found in which the calcified lymph nodes perforate the bronchus and are coughed out by the children. Huebschmann's [52] opinion was pessimistic, also. On the contrary, Weigert and Ghon [53] emphasized that besides cases of severe bronchial rupture there are also cases of a moderately severe nature and that even cases of a mild character are to be found. Rössle [12] divided bronchial stenosis in two groups: (1) the clear form and (2) the obscure form. He stated that the prognosis for the "clear form" is always good, for it results from exterior pressure on the bronchus from the enlarged lymph nodes, while the prognosis for the obscure is not so favorable, for in these cases a caseous lymph node penetrates into the bronchus and causes bronchial spread, formation of cavity or caseous pneumonia.

Since systematic examinations of bronchial rupture have been carried out, increased attention has been given to the postmortem examinations for bronchial ruptures in the case of every child who has died of tuberculosis. Postmortem examinations made at the St. James Hospital by pathologist A. Kálló are made in such a way that the trachea and all the bronchi are carefully opened with scissors, utmost care being taken that none of them be injured during the opening. More detailed examinations will be reported in a later work; at present we only state that postmortem examination revealed bronchial rupture in 8 (47.1 per cent) of 17 cases of tuberculosis among children. This figure is much higher than any hitherto published. It is evident that the number of our cases is not high, but we hope that there will be no great differences in the ratio in the future. The cause of this high

57. Müller, R. W.: Ztschr. f. Tuberk. **82**:214, 1939.
58. Hamburger: Deutsche Ztschr. f. Tuberk. **10**:120, 1942.
59. In Engel and Pirquet.[5]

percentage is to be sought in careful technic, for the recognition of bronchial rupture is not always so simple as it is generally believed to be. Sometimes only a little opening is found through which the content of the caseous lymph node expands into the lumen of the bronchus. In other cases bronchial rupture is accompanied by such a great destruction of the wall of the bronchus that bronchial rupture is easily recognizable. As has been stated, we will give details concerning these investigations in the future.

The results of the pathologic examinations do not represent the actual situation because most of the children die before bronchial rupture would set in. At necropsy most tuberculous children were found to have tuberculous meningitis, and it is well known, according to the reports of Ghon,[58] Engel,[59] Wallgren [60] and Hamburger,[61] that tuberculous meningitis is one of the earliest complications of primary tuberculous infection; it sets in in 90 per cent of cases from three to six months after the primary infection. Rupture of caseous lymph nodes usually occurs a little later, except in babies and young children, so that we may say that if children with tuberculous meningitis had lived longer the bronchial rupture would probably have occurred. At postmortem examinations of tuberculous children who did not die shortly after the primary infection, but only later (of chronic miliary tuberculosis, peritoneal tuberculosis, etc.) we almost regularly found various forms of bronchial rupture even then, although the serious tuberculous process was not located in the lungs.

At postmortem examination we found 9 cases of bronchial rupture at the White Cross Hospital and 8 cases at the St. James Hospital. Among these 17 cases the primary focus ruptured into a bronchus three times. Besides the rupture of the primary focus a lymph node at the bifurcation ruptured into a main bronchus in 1 case. A double bronchial rupture occurred in 2 cases. The incidence of double bronchial rupture cases noted at our postmortem examinations was 17.6 per cent.

The places where the rupture had taken place in the different bronchi were as follows: secondary and tertiary bronchi, 6 cases (5 of them into the lower lobes); primary bronchus, 6 cases (2 into the middle and 2 into the lower lobes); main bronchus, 4 cases, and trachea, 1 case. We therefore worked out this material carefully in order to learn in how many cases we would have been able to find the rupture by means of bronchoscopy. Ruptures into the trachea or in the main bronchi were distinctly visible. Of the 6 cases in which the rupture

60. Wallgren, S.: Acta pædiat. **17**:150, 1935.

61. Hamburger, F., and Dietl, K.: Die Tuberkulose des Kindesalters, ed. 3, Vienna, Franz Deuticke, 1932.

occurred into the primary bronchi it was visible in only 4 cases, because one cannot look into the upper lobes with the bronchoscope. Of the 6 ruptures into the secondary and tertiary bronchi 5 occurred in the lower lobes, but it is rather difficult to find the place of the rupture in these small bronchi, especially when they are far from their origin. In only 9 cases of 17 cases (52.9 per cent) in which there was postmortem examination could the location of the rupture have been found by means of a bronchoscope. For the time being we have to come to the conclusion that the number of bronchial ruptures is much higher than bronchoscopy can prove. This can be proved even by our case 12, in which bronschoscopy gave a negative result, while the postmortem examination one month later showed rupture into the bronchus of the upper lobe of the right lung. Now it is comprehensible why we made examinations in cases in which only slight signs of atelectasis were found and in which significant signs of bronchial stenosis were lacking: We were anxious to see the limits of the capacity of bronchoscopy, but in most cases we obtained a negative result. Ruptures in small bronchi cannot be found. A negative bronchoscopic result therefore does not exclude the possibility of ruptures into smaller bronchi.

At autopsy in our more recent cases we carefully examined the consequences of the bronchial rupture. As has already been said, pathologists are pessimistic concerning the prognosis for bronchial rupture, especially because they see great danger in its consequences. Bronchial rupture occurred in 62.5 per cent of our cases without any harmful consequences, because we did not find any traces of consequences of bronchial rupture in the lungs in 5 of the 8 cases in which we made careful examination. We found 1 case of caseous pneumonia and 2 cases of bronchogenic spread, but they were not of such a dangerous nature that they could not have been cured. Clinicians like Simon,[17] Redeker,[8] and R. W. Müller [62] have long emphasized that a part of the bronchogenic spread which follows bronchial rupture disappears later in roentgenograms, which shows that cure is possible. The number of cases in which we made postmortem examination is too small to be conclusive, but they permit the tentative assumption that the prognosis for bronchial rupture is not in the least so poor as is generally believed, because most bronchial ruptures have no complications, and even complications do not always prove fatal, for many of them can be healed.

We did not collect cases in which the lymph nodes had narrowed the bronchi and in which no rupture had taken place. Tubes carefully examined at autopsy frequently show arched lymph nodes. In these cases lymph nodes coalesce with the wall of the bronchi and, while

62. Müller, R. W.: Beitr. z. Klin. d. Tuberk. **95**:108, 1940.

destroying it, they encroach on the lumen. Such protuberances are often to be seen at bronchoscopy (Kilian,[28] Schrotter,[30] Paunz [45] and others). We ourselves observed them in 3 cases (cases 19, 20 and 21). These protuberances occurred only when the lymph node had previously coalesced with the wall of the bronchus and had partly destroyed it. The encroaching of the lymph nodes can therefore be considered the prelude of the rupture. This is proved by the fact that the caseous content of the lymph node is often visible through the mucous membrane. "Compressive stenosis," a term commonly used in the literature, is only the introductory phase of bronchial rupture. The intrathoracic lymph nodes act like the lymph nodes in the neck, which coalesce with the skin and destroy it as long as they can get rid of their caseous content and find the exit through the skin. The same distinctly visible pathophysiologic course is followed by the intrathoracic lymph nodes: growing together with the bronchi, destroying their wall and even their cartilage in order to penetrate into the bronchi to get rid of their caseous content. The same pathophysiologic process takes place in cases of periproctal abscesses: the abscess penetrates into the rectum to get rid of its purulent content.

Naturally not all caseous lymph nodes in the neck perforate the skin and not every intrathoracic lymph node perforates the bronchi, especially when caseation is not advanced, but the tendency to do so is always present. We therefore must state that bronchial rupture belongs to the phenomena occurring every day, for this is the pathophysiologic way for the lymph nodes to empty their caseous masses. This is proved by cases in which spontaneous evacuation of these caseous masses was observed. We have already mentioned that the first child whose survival was reported (by Oekonomides [25]) after bronchial rupture had freed itself spontaneously of the caseous masses by coughing them out. Spontaneous evacuations were reported in 1904 by Jundell [63] in the case of a boy 11 years old. In 1932 Malmberg [41] reported the same occurrence in a boy 4 years old. In a case described by Düggeli [16] in 1942 a 26 year old man five months after his primary tuberculous infection coughed out 50 cc. of yellowish green material from which tubercle bacilli were isolated; roentgen examinations showed atelectasis in the upper lobe of the left lung. The number of such cases is much higher than generally believed, but they have not yet attracted the physician's attention sufficiently. We observed a 3 year old boy in 1943 who five months after his primary tuberculous infection suffered slight attacks of dyspnea and in whom at roentgen examination atelectasis of the middle lobe of the right lung was found. Two weeks later his mother told us that coughing and dyspnea had

63. Jundell, I.: Jahrb. f. Kinderh. **60**:76, 1904.

ceased when the child during the course of a few days had coughed out a "rubber-like" mass which she had failed to show us. Further roentgen examinations at this time proved disappearance of the atelectasis.

It is a well known fact that lymph nodes empty not only their caseous but even their calcified content through the bronchi. We have already mentioned that Beitzke [59] the pathologist observed at autopsy cases in which calcified masses had perforated the wall of the bronchus. Fleischner [64] in 1935 reported 3 cases in which there was penetration of calcified lymph nodes into the bronchus causing atelectasis in some lobes; when the calcified masses had been coughed out, the atelectasis disappeared. We suppose that such cases occur much more frequently than is generally believed. We must remember that cases in which evacuation of such masses occurs may show clinical symptoms so mild that they can easily be overlooked by the physician. Only the most striking cases are noted, for general medical knowledge on this question has been left far behind hitherto. The more physicians consider such possibilities the more they will observe them in the future.

By description of cases with bronchial rupture authors try to find an explanation why this could have happened. It is supposed that measles or some grippal infections are contributive factors. The possibility of these contributive factors cannot be denied, though in our 18 cases with bronchial rupture neither measles nor any grippal infections were to be detected in the anamnesis, and yet the bronchial rupture set in. The explanation of this is that the lymph nodes, following their pathophysiologic course, had tried to evacuate their superfluous content through the bronchi.

Clinical, roentgenologic and bronchoscopic observations clearly indicate the different phases of this pathophysiologic course, and we can firmly assert that the clinical and roentgen manifestations of the primary tuberculous infection mostly represent nothing other than the different phases of this pathophysiologic course.

We thought it interesting and from the practical aspect important to determine the lapse of time between the manifestation of the primary tuberculous infection and the bronchial rupture.

To determine this is not at all easy, for it is rather difficult to state when the primary tuberculous infection occurred. Decades ago Wallgren observed cases with erythema nodosum, for the appearance of the cutaneous eruptions is the manifestation of primary tuberculous infection, indicating simultaneously the development of tuberculous allergy. Up to the present we have had no opportunity to observe cases of erythema nodosum which were followed later by bronchial rupture;

64. Fleischner, F.: Beitr. z. Klin. d. Tuberk. **86**:72, 1935.

therefore we took into consideration the appearance of initial fever or the time when the reaction to the tuberculin test became positive. Cases in which this time can be exactly determined are rare in the literature, and only 16 cases could be collected, partly from the literature and partly from our own material. Only cases which were submitted to the most severe critical examination and cases with perfectly reliable data were admitted to this list. Sixteen cases are not too many, but still they are informative. As table 2 shows, bronchial rupture set in mostly within four to six months after the manifestation of primary tuberculous infection. A certain regularity seemed to rule, for even in some infants and in a single adult bronchial rupture was noticeable in this time. The younger the children are the earlier the bronchial

TABLE 2.—*The Lapse of Time Between the Manifestation of Tuberculous Infection and Bronchial Rupture*

No.	Author	Year	Age of Child	Lapse of Time	Comment
1	Widerhofer and Frühwald (cited by Ebert [27])	1885	4 yr.	3 yr.	Peritonitis, tuberculosis
2	Loeb [65]	1886	4 yr.	6 mo.	
3	Jundell [63]	1904	11 yr.	5 mo.	
4	Orel [48]	1933	6 yr.	8 mo.	
5	Orel [48]	1933	7 yr.	17 mo.	Often feverish
6	Spivek [49]	1936	10 mo.	5 mo.	
7	Spivek [49]	1936	3 yr.	17 mo.	Tuberculosis of lymph nodes in the neck
8	Spivek [49]	1936	4 yr.	14 mo.	
9	Spivek [49]	1936	7 mo.	4 mo.	
10	Faust [47]	1936	11 mo.	3 mo.	
11	Düggeli [16]	1942	26 yr.	5 mo.	
12	Görgényi-Göttche and Kassay	1945	4 yr.	6 mo.	
13	Görgényi-Göttche and Kassay	1945	4 yr.	6 mo.	
14	Görgényi-Göttche and Kassay	1946	8 wk.	6 wk.	
15	Görgényi-Göttche and Kassay	1946	5 yr.	5 mo.	
16	Görgényi-Göttche and Kassay	1946	2 yr.	5 mo.	

Bronchial rupture followed after 0-4 mo. in 3 cases; 4-6 mo. in 8 cases; 6-12 mo. in 1 case; 1-1½ yr. in 3 cases; 2-3 yr. in 1 case

rupture will set in, as is proved in our frequently mentioned case 6, in which bronchial rupture took place after six weeks. Bronchial rupture can also occur later, but in such cases the course of the primary tuberculous infection usually shows some complications. In table 2 4 cases were collected in which bronchial rupture set in after more than four to six months, and in 3 cases complications were found. This question cannot be given a final answer on the basis of so few cases, but for the time being we can say only that except in infants in cases of primary tuberculous infection without any complications one must consider the possibility of bronchial rupture within four to six months after the appearance of allergy.

The pathologic and bronchoscopic examinations clearly showed that several bronchial ruptures may occur, in different bronchi. These bronchial ruptures do not necessarily occur at the same time; thus one

must consider the possibility that a bronchial rupture may be followed by another rupture. We have made some observations concerning this matter, but they are not exact enough to stand a severe critical examination. However, if cases are carefully observed it will be found that multiple bronchial rupture is not a rarity.

Caseation in the lymph nodes develops in the following manner: 1. Necrosis: Caseation begins in the inside of the lymph nodes. Therefore the tuberculous granulation tissue remains in its living state longest in the neighborhood of the capsule. 2. The caseous necrotic tissue is at first coherent and almost elastic. 3. Later it falls into a crumbling mass. 4. Finally it softens, and the whole lymph node is metamorphosed into a cold abscess.

If there is tuberculous granulation tissue around the capsule of the lymph nodes, then, having perforated the wall of the bronchus, it appears first in the lumen of the bronchus. This process can take place without any pronounced clinical symptoms: The appearance of the granulation tissue in the lumen of the bronchus usually causes mild and slowly developing clinical symptoms, because this granulation tissue gets into the lumen only in small measure. When the granulation tissue gets into the small tube of an infant obstructive emphysema may result, or it may even lead to atelectasis.

If the lymph node perforates the bronchus when its content is coherent and elastic, bigger pieces, difficult to cough out, may get into the tubes. Here they can cause sudden death by obstruction of the trachea or the main bronchi or by being wedged into the larynx. The older physicians scarcely knew of any other type than this. Therefore it is this type that is found described especially in the works of Loeb[65] and Ebert.[27] The effect of these larger elastic pieces closely resembles that of aspirated foreign bodies as in our cases 1 and 5, in which we supposed foreign bodies had been aspirated before we tried bronchoscopy. If these bigger caseous masses obstruct the bronchi for a longer time inflammation can develop, followed by bronchiectasis, as in cases of aspiration of foreign bodies. These coherent elastic masses form a mechanical obstacle and in this case are dangerous, but they do not play a large part in the bronchogenic spread of the tuberculosis.

If the caseous mass crumbles, it may be coughed out or aspirated by the child. These small masses can even get into the smaller bronchi, causing bronchial spread. Most severe bronchial spread is to be feared as the result of opening of a cold abscess. The softened mass can similarly obstruct the bronchi, causing sudden death. The effects chiefly depend on how large the opening of the bronchial rupture is, how much of the necrotic masses gets into the tubes at once and in what measure

65. Loeb, M.: Jahrb. f. Kinderh. **24**:353, 1886.

the child is able to cough them out. The prognosis is quite different in cases in which the lymph nodes empty their caseous content slowly through a small opening into the tubes, where it can be coughed out easily, and in cases in which big caseous masses pour in great amount into the tubes, causing sudden attacks of dyspnea and different obstructions. We see that bronchial rupture may sometimes be very dangerous, but fortunately in practice it is seldom fatal, for bronchial rupture according to its frequency is a benign process which in the majority of cases is followed by complete recovery, because children are able to cough out the caseous masses completely, even if startling clinical symptoms are sometimes encountered. Physicians are only beginning to know about bronchial ruptures; if they gain a better knowledge of the pathologic picture of bronchial ruptures, then they will become aware that the hitherto published literature mostly dealt with "alarming" cases, which were so striking that they could not be overlooked. The better the clinical and roentgen signs of these pathologic pictures are known, the better it will be seen that besides "alarming" cases there are "striking" and even "silent" cases and that the latter are in the majority.

With respect to the clinical and roentgen symptoms of bronchial rupture we emphasize that we saw nothing that was not observed before by other researchers, but according to our experiences the consideration of these symptoms does need a little revision. It is a well known fact that in cases of bronchial rupture the children's cough is of various types. This cough is sometimes persistent, irritative and annoying and frequently occurs in paroxysms which in many respects resemble those of pertussis. Hence since the time of Baréty [66] it has been called "coqueluchoid" (pertussoid), but it is not accompanied by the expectoration of a mass of tenaceous mucus. These paroxysms are severe and prolonged. The cough often has a curious "ringing brassy character" which is readily recognizable, and it has been described as a "bitonal cough." The irritative cough appears mostly at the beginning of the bronchial rupture, when only the lumen of the bronchus is narrowed, but when the "ringing brassy" or the "bitonal" sounds are heard, they indicate that foreign bodies in the lumen cause the change of the cough's character. These phenomena were explained formerly by the irritation of the "tussogene zone." This assumption may be adopted in cases of irritative cough but not in cases in which the character of the cough is changed. It is imaginable only that in these cases foreign bodies are in the tube which are able with their variable vibration to

66. Baréty, A.: De l'adenopathie trachéobronchique, en général et en particulier dans la scrofule et la phthisie pulmonaire, précédée de l'étude topographique des ganglions trachéobronchiques, Paris, A. Delahaye, 1874.

add various tonal nuances to the cough. These foreign bodies are granulation tissue or pieces of caseous material. We regard ringing brassy or bitonal cough as a result of bronchial rupture. Observation of breathing is important. Attacks of dyspnea, when the child becomes cyanotic and breathing becomes difficult, are of such an alarming nature that they are recognizable to every one. In these cases the tubes are entirely filled with caseous material, which makes an immediate bronchoscopy necessary. But there are cases in which the strained breathing is recognizable only by an expert. The strained breathing is especially pronounced during walking and even more during running and during more strenuous physical exertion. In our case 9 the girl, 7 years old, was brought to us with the complaint that during the previous three weeks she easily became tired and that while hurrying she tended to suffocate and her heart began to beat strongly. The child's parents and her physician both suspected a disorder of the heart until roentgen examination revealed that the cause of the strained breathing was bronchial stenosis, which, according to bronchoscopy, was caused by bronchial rupture. An important symptom is the rattling and whistling of the lungs during expiration. Jackson [67] in 1918 described the whistling and named it "asthmatoid wheeze" especially well heard when the mouth is open. This wheeze is an important sign, but it is also audible when granulation tissue begins to grow into the lumen of the bronchi. The so-called expiratory rattle, described by Schick [68] in 1910, is to be considered significant only when it appears at the same time with the strained breathing, for a single rattle is to be heard in cases of simple bronchitis or bronchiectasis. When expiratory rattle is heard with strained breathing it indicates that masses are in the tubes which are to be removed by bronchoscopy. Such an expiratory rattle was especially pronounced in our case 11: The 5 year old boy came to us with the complaint that, though he was well, he coughed a little and when moving fast there was a loud rattle. Bronchoscopy revealed that the right main bronchus was filled with caseous masses which were lentil, pea or bean sized (fig. 11 *B*). Thus the origin of the rattle was clearly visible.

Some comment seems necessary concerning the temperature in cases of bronchial rupture, because here opinion differs greatly. We read about cases in which bronchial rupture was preceded by high temperature and cases in which there was no fever during the whole process, and we also know of cases in which fever appeared only after bronchial rupture. According to our experiences all these three possibilities exist. To recognize the true situation it is not enough to consider the tempera-

67. Jackson, C.: Am. J. M. Sc. **156**:625, 1918.
68. Schick, K.: Wien. klin. Wchnschr. **23**:153, 1910.

ture, but it is most necessary to observe the activity of the whole tuberculous process concerning the changes in sedimentation rate. Regarding these circumstances we can establish three types:

1. The child is constantly feverish before the bronchial rupture, and the sedimentation rate is steadily high. These circumstances were found in our cases 3, 6 and 12, whereas in our cases 5 and 18 the temperature was normal but the sedimentation rate was high. These are the cases in which bronchial rupture followed a constant active tuberculous process which made fever and a high sedimentation rate comprehensible. Cases of severe disease are to be considered in which there is active tuberculosis of the endothoracic lymph nodes, for bronchial rupture is only a phase of this process. Our case 6 had a fatal outcome because of perforation of the bronchus by a caseous lymph node, which was followed by a perforation of the esophagus. Case 12 was also fatal, because of tuberculous meningitis which followed one month after the bronchial rupture. The prognosis of these cases had to be poor even if bronchial rupture had not taken place, on account of the active tuberculosis of the lymph nodes. Double bronchial rupture often develops in such cases, as is shown in case 5, and under these circumstances a bronchogenic spread is mostly to be feared.

2. In most cases the bronchial rupture is not preceded by fever, and the sedimentation rate is constantly low, as in cases 4, 7, 8, 10, 11, 13, 14, 15, 16 and 17, which means 61.1 per cent of our cases. In these cases the bronchial rupture set in when the process had begun to abate. These cases show best that the tendency of bronchial rupture is nothing but evacuation of the superfluous necrotic content of the lymph nodes.

3. In this type of case fever appears during or after the bronchial rupture (cases 1 and 2). Here the caseous masses obstructing the main bronchus, like foreign bodies, may cause inflammation behind the obstructed bronchus, or bronchogenic spread develops. According to our experience the obstructing caseous masses often cause more or less inflammation either in the bronchi or in the lung, which is followed by bronchiectasis.

We do not wish to dwell at length on bronchogenic spread. We only emphasize once more that it is not nearly so dangerous as is generally believed. Here we mention only that bronchogenic spread often occurs in the atelectatic areas of the lungs, mostly in the neighborhood of the bronchial rupture. It is therefore advisable when the child is feverish a long time and roentgen examination does not show anything but constant homogenic shadow in the lung, to suggest the possibility of a bronchogenic spread in the atelectatic area.

In the diagnosis of bronchial rupture roentgen examination is of definite importance. The roentgen examination in these cases is origi-

nally an indirect procedure, because bronchial rupture is invisible; it is the bronchial stenosis which is visible.

Among the roentgen symptoms of bronchostenosis we emphasize the prior importance of the Holzknecht-Jakobson sign. Table 1 containing all our cases indicates clearly in every case whether the Holzknecht-Jackobson sign was present or absent. Essential for the Holzknecht-Jakobson sign is the fact that the mediastinal organs during deep inspiration move to the side where bronchial stenosis exists. This sign is present only when stenosis is developed in a high degree and located in a main bronchus. The moving of the mediastinal organs means that on the side toward which they are moving the main bronchus is narrowed. If there is stenosis in the smaller bronchi the moving of the mediastinal organs does not occur. The Holzknecht-Jackobson sign was found in 15 cases. Bronchoscopy was done in all cases and in 14 cases bronchial rupture was discovered, whereas only 1 case showed a considerable encroachment of a lymph node into the lumen. According to our experiences bronchoscopy ought to be done in all cases in which the Holzknecht-Jakobson sign is present, because in most such cases a bronchial rupture already exists. The Holzknecht-Jakobson sign is sufficient reason to perform bronchoscopy even if it is the only sign of bronchial stenosis. Bronchoscopy was done in our cases 9, 10 and 11, and indeed bronchial rupture was at hand. On the other hand, if the Holzknecht-Jakobson sign is absent, existence of a bronchial rupture is not excluded. In such cases other signs call attention to the bronchial rupture. For instance, in our case 5 the Holzknecht-Jakobson sign was absent, since here a double bronchial rupture into the right and into the left main bronchus had taken place, preventing the mediastinal organs from moving in either direction. The Holzknecht-Jakobson sign was absent in case 6, also, in which the obstructive emphysema on the left side was so far advanced that the mediastinal organs were entirely crowded to the right side. These were striking exceptions to the rule. The main task is carefully to observe at every roentgen examination whether the Holzknecht-Jakobson sign is present or not, because this sign is the most reliable in the diagnosis of stenosis of the main bronchi.

Finally, we should like to say a few words about the question of obstructive pulmonary emphysema. Obstructive pulmonary emphysema develops, as is known, when one of the main bronchi is partly stenosed and air can get in by inspiration but does not get out at expiration; it therefore accumulates in the lung, and emphysema develops. The lung behind the stenosis is widened, the intercostal spaces are enlarged, the diaphragm is pressed down, and the mediastinal organs move to the normal side during expiration.

The roentgen signs of obstructive pulmonary emphysema were described by Arnsberger [33] in 1909 and by Ziegler [34] in 1913. They

observed this pathologic picture mostly as a result of aspiration of a foreign body. This pathologic picture slowly enters into the general medical knowledge, which is characterized best by the fact that Spivek [49] could collect only 18 cases of obstructive pulmonary emphysema caused by bronchial rupture of tuberculous lymph nodes from the whole literature up to 1936. Spivek [49] himself added 4 cases to the collection. In the same year 1 case was reported by Faust.[47] During the last two years we observed 4 cases of obstructive emphysema, cases 6, 7, 8 and 13. Of these case 13 was conspicuous, like those published in the literature; the rest were much less noticeable, but even these cases ought to be considered. In all our cases bronchoscopy was done, and in all these cases there was bronchial rupture. In 3 of our 4 cases the Holzknecht-Jakobson sign was present. According to this, the mediastinal organs moved during inspiration to the stenosed side and returned during expiration.

In some cases it is rather difficult to find whether there is obstructive pulmonary emphysema on the right side or atelectasis on the left side, because during expiration the mediastinal organs may be shifted so strongly to the normal side (as in our case 6) that they cannot return to the affected side, because the accumulated air makes backward movement impossible. In these cases the situation can be confirmed by auscultation, because on the affected side no breath sounds are audible. In cases of obstructive pulmonary emphysema the breathing above the affected lung is diminished in such degree that it canot pass unnoticed.

The importance of bronchoscopy cannot be denied. The bronchoscope used as a diagnostic instrument becomes an important therapeutic instrument in the moment when the parts of the ruptured lymph nodes in the lumen of the bronchus are discovered, for they need immediate removal, naturally without injury to the wall of the bronchi. We have spoken already about how much damage this material can do: It may hinder the breathing, it may obstruct the bronchi, thereby causing inflammation followed by bronchiectasis; it may be the source of bronchogenic spread, and, finally, it may lead to suffocation. Therefore the masses in the bronchi are to be removed immediately and radically.

The material which fills the lumen of the bronchus is loosely connected with the wall of the bronchus or with the lymph node; therefore it may easily be removed with adequate instruments (such as tweezers or curet). In many cases the material is spontaneously coughed out through the tube of the bronchoscope.

The removing procedure is not dangerous, because the necrotic granulation tissue or the caseous masses do not bleed and the freed pieces are easily removed. In all our cases the removal of the masses was useful and mostly was followed by quick and definite recovery (cases 1, 7, 8, 9, 11, 13, 14, 15 and 16). Improvement occurs even

if only a part of the mass is removed, because thus the way is opened for total evacuation of the lymph node, as is shown in our case 10.

We do not go into details about the technic of bronchoscopy. We should only like to say what we demand from the use of bronchoscopy: First, the procedure should not be dangerous. Second, its use should cause no injury to the child and ought to be painless. We maintain that all this is possible. It is important, because we do not advise a procedure which brings with it danger or pain or injury, for we have to weigh whether the benefit or the danger is greater.

There are few contraindications against bronchoscopy. When the child suffers with acute pharyngitis, laryngitis or tracheobronchitis with fever, bronchoscopy is to be postponed because the inflammation may be transported to the lower parts of the respiratory tract. Bronchoscopy is to be postponed also in cases of other acute illnesses like scarlet fever, typhoid or phlegmon, except in cases in which suffocation threatens and demands immediate operation. Fever caused by a tuberculous process is not a contraindication; on the contrary, the removal of the masses helps the organism to recover except when hematogenic spread already exists—it is doubtful whether bronchoscopy can do any good to the child who is naturally weakened by the hematogenic spread.

Children with exudative diathesis should be carefully treated on account of the possibility of laryngeal edema.

The children are narcotized before we start bronchoscopy. Recently we have been giving chloral hydrate (1.5 to 2.5 Gm. of 5 per cent solution orally) to children under 5 years old half an hour before bronchoscopy is started. In most cases we need not give any other narcotics, because chloral hydrate makes the children sleep soundly; thus bronchoscopy can be performed quietly. Children more than 6 years old get, besides the chloral hydrate, an easy superficial ether narcosis. Jackson [56] recommended bronchoscopy without anesthetics. We sometimes performed bronchoscopy in this way, but we are convinced that bronchoscopy made with the patient in narcosis is carried out in a shorter time and causes no pain to the children.

We always introduce the tube through the larynx. This can be carried out with very small babies (case 6) without injury of the mucous membrane of the glottis. It is usually advisable to perform bronchoscopy as quickly as possible, and the tube in the glottis should also be left there as short a time as possible, for if the tube remains longer in the glottis laryngitis may develop with sometimes severe consequences, which may even necessitate immediate tracheotomy. Without dealing any further with the details of bronchoscopy, we should like to emphasize the fact that bronchoscopy done in children is a harmless procedure. Therefore, when it is necessary, we vote for it without any reservations.

SUMMARY

In the course of the past two years we have observed bronchial rupture by bronchoscopy in 18 children, and at autopsy 8 children with bronchial rupture were found. We arrived at the following conclusions:

At autopsy of tuberculous children we have found bronchial rupture in 47.1 per cent of cases by the use of a specially careful technic. This percentage is much higher than all hitherto published figures in the literature. We had double bronchial rupture in 17.6 per cent of our cases. The 52.6 per cent of bronchial ruptures was proved by bronchoscopy. Many ruptures occur in smaller bronchi which cannot be reached with the bronchoscope.

The prognosis of bronchial rupture is not nearly so poor as is popularly believed, for in our cases in which autopsy was performed 62.5 per cent did not show malignant consequences, and the same result was shown in 77.7 per cent of cases in which bronchoscopy was done. The bronchial rupture is to be considered a relatively common and benign pathophysiologic process. The tuberculous lymph nodes are trying to evacuate their necrotic superfluous content into the bronchi where it should be removed by coughing, the organism thus being relieved of it. This pathophysiologic course is shown by the fact that spontaneous evacuation from the bronchus of caseous and even calcified parts of lymph nodes takes place through coughing; this was reported in the literature long ago, and it happens much more frequently than is commonly believed. The clinical and roentgen diagnosis of primary tuberculous infection is actually occupied with nothing but the different phases of this pathophysiologic process. The bronchial rupture takes place four to six months after manifestation of primary tuberculous infection, and with small babies it can set in even earlier.

The cough of "ringing brassy" or "bitonal" character indicates that in the bronchi there is at least granulation tissue which acts like a second glottis and with its different vibration adds a variable sound to the cough. The "asthmatoid wheeze" and the "expiratory rattle" originate from granulation tissue or caseous masses which have penetrated into the bronchi.

If the child is constantly feverish before the bronchial rupture and if the sedimentation rate is steadily high, then the bronchial rupture occurs on account of the active tuberculous process of the lymph nodes. In these cases the disease is to be considered severe not on account of the bronchial rupture but on account of the tuberculous process. In these cases multiple bronchial rupture often develops; these ruptures are usually followed by bronchogenic spread.

In 61.1 per cent of our cases the children were feverless before the bronchial rupture and the sedimentation rate was constantly low. These cases show most clearly that the aim of bronchial rupture is nothing

but the evacuation of superfluous content of the caseous lymph nodes. If fever develops after bronchial rupture it is caused either by occlusion of the bronchi, which causes inflammation as from aspiration of foreign bodies, or by bronchogenic spread.

For the diagnosis of bronchial rupture roentgen examination is of main importance. Among the roentgen signs the Holzknecht-Jakobson sign is the most valuable, for it indicates that on the side to which the mediastinal organs move during inspiration the main bronchus is severely stenosed. Among our 15 cases in which the Holzknecht-Jakobson sign was present we found bronchial rupture in 14 cases; in 1 case an encroachment of the caseous lymph nodes onto the bronchus was found. The Holzknecht-Jakobson sign gives an imperative indication for bronchoscopy.

Obstructive pulmonary emphysema is much commoner than is generally believed, and it is an imperative indication for bronchoscopy.

Since bronchoscopy performed in children and even in infants is a harmless procedure, it ought to be done in any case in which there is suspicion of bronchial rupture. Not only is it useful for diagnosis, but it is an important therapeutic procedure which removes the caseous masses from the bronchi and is often of lifesaving importance. Bronchoscopy is an important procedure which cannot be spared in pediatric practice.

Case Reports

CONGENITAL HEART DISEASE
Complete Transposition of the Great Cardiac Vessels

FLORENCE E. LAWSON, M.D.
CHICAGO

ABBOTT [1] described transposition of the arterial trunks as that condition in which "the great trunks have undergone an alteration in their relative position to each other or to the ventricles from which they emerge whereby the aorta comes to lie in the path of the unaerated blood from the right ventricle." This definition includes four types of anomalies: overriding aorta; partial, or simple, transposition; complete, or crossed, transposition; mixed transposition, or transposition with atresia of the valves.

It is the purpose of this paper to present a case of complete transposition of the arterial trunks in which the aorta arose from the right ventricle and the pulmonary artery from the left ventricle.

Many theories have been advanced to explain the abnormality; these have been reviewed by Lev and Saphir.[2]

Kürschner,[3] in 1837, stated that transposition of the vessels occurred because of failure in the spiraling of the great vessels and faulty fusion of the septums of the ventricle and the truncus.

Von Rokitansky,[4] in 1875, disagreed as to a correlation between the spiraling of the great vessels and the direction of the lower truncus septum. He emphasized the possible importance of defects in anlage and in the development of the truncus septum.

Spitzer,[5] in 1919 and 1921, advanced the phylogenetic theory. If the usual 180 degree clockwise rotation of the conus arteriosus fails to

From the Department of Medicine, Northwestern University Medical School, and the Wesley Memorial Hospital.

1. Abbott, M.: Atlas of Congenital Cardiac Disease, New York, American Heart Association, 1936.

2. Lev, M., and Saphir, O.: Theory of Transposition of Arterial Trunks Based on Phylogenetic and Ontogenetic Development of Heart, Arch. Path. **39**: 172-183 (March) 1945.

3. Kürschner, T.: Commentatio de corde cujus ventriculi sanguinem inter se communicant, Marburgi, 1837; cited by Harris and Farber.[6]

4. von Rokitansky, C. F.: Die Defecte der Scheidewande des Herzens, Vienna, W. Braumüller, 1875; cited by Harris and Farber.[6]

5. Spitzer, A.: Arch. f. Entwcklngsmechn. d. Organ. **47**:511-570, 1920-1921; cited by Harris and Farber.[6]

occur, the aorta arises from the right side of the heart. Spitzer expressed the opinion that right-sided aorta represents a persistence or reopening of the right-sided aorta of the reptilian heart.

Harris and Farber,[6] in 1939, reviewed the various hypotheses and presented evidence to support the Spitzer theory. Further support came in 1941, when Liebow and McFarland[7] reported a case of rudimentary right-sided aorta.

In 1942, as a result of embryologic study, Bremer[8] presented the view that transpositions of the great arteries are the result of some slight variation in the normal course of embryonic development.

The occurrence of complete, or crossed, transposition of the great vessels is relatively rare. Abbott[1] presented 49 cases of complete transposition, in 32 of which there was a closed ventricular septum. Analysis of these cases was presented by Bauer and Astbury.[9] Gibson and Clifton[10] noted 9 cases in a series of 105 congenital cardiac anomalies. Emerson and Green[11] presented 12 cases in a series of 29 cases of various types of transposition of the great vessels. In 11 of these 12 cases a patent foramen ovale was present.

The life expectancy of patients with complete transposition of the great vessels with closed septums is only a few weeks. The highest age recorded by Abbott[1] is 11 years. When there is a patent foramen ovale, the patient may reach adulthood. Carns and associates[12] presented a case of a woman with this anomaly who lived 44 years.

REPORT OF A CASE

A girl aged 5 years was admitted to Wesley Memorial Hospital, Chicago, Nov. 24, 1940, to the service of Dr. Gilbert H. Marquardt, with congenital heart disease and bronchopneumonia. At this time a complete history from birth was taken.

The mother stated that weight at birth was 8 pounds (3,629 Gm.) and that the child had been normally pink and white until she was 2½ months old. Slight

---

6. Harris, J. S., and Farber, S.: Transposition of Great Cardiac Vessels, with Special Reference to Phylogenetic Theory of Spitzer, Arch. Path. **28**:427-502 (Oct.) 1939.

7. Liebow, A. A., and McFarland, W.: "Corrected Transposition" and Persistent Rudimentary "Right Aorta" as Evidence in Support of Spitzer's Theory, Arch. Path. **32**:356-368 (Sept.) 1941.

8. Bremer, J. L.: Transposition of the Aorta and Pulmonary Artery: Embryologic Study of Its Cause, Arch. Path. **34**:1016-1030 (Dec.) 1942.

9. Bauer, D. de F., and Astbury, E. C.: Am. Heart J. **27**:688-732, 1944.

10. Gibson, S., and Clifton, W. M.: Congenital Heart Disease: Clinical and Postmortem Study of One Hundred and Five Cases, Am. J. Dis. Child. **55**:761-767 (April) 1938.

11. Emerson, P. W., and Green, H.: J. Pediat. **21**:1-22, 1942.

12. Carns, M. L.; Ritchie, G., and Musser, M. J.: Am. Heart J. **21**:522-529, 1941.

clubbing of the fingers and cyanosis were noted at this time, becoming gradually more apparent until, at the age of 7 months, dyspnea was observed. At 8 months she had rubella. At the end of the first year she weighed 18 pounds (8,165 Gm.). When she was 2 years old, she had a severe cold, during which the cyanosis became deeper. During the next year her abdomen became enlarged; she was digitalized and given three months' rest in bed. Her condition improved until, at the age of 5, she contracted pneumonia, which necessitated the hospitalization here reported.

On examination, the blood pressure was 80 systolic and 50 diastolic and the weight 32 pounds (14.5 Kg.). The child was poorly developed, and the skin and mucous membranes were reddish, blue. Prominent pulsations in the neck were noted. Examination of the lungs revealed a condition typical of bronchopneumonia. The heart was enlarged to the right, with a rate of 136 beats per minute and sinus rhythm; no murmurs were heard. The liver was enlarged. There was prominent

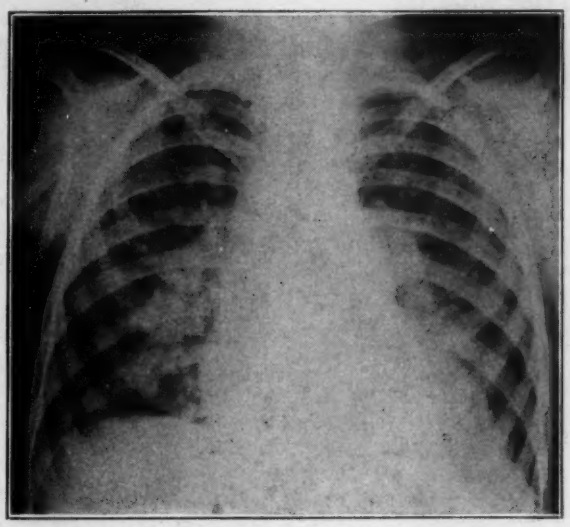

Fig. 1.—Roentgenogram of the chest taken at a distance of 2 meters, showing transposition of the great vessels. The heart increased 3.3 cm. to the right border and 17.6 cm., to the left border and 18 cm. in total transverse diameter.

clubbing of the fingers and toes. The red blood cell count was 9,110,000, with 28 Gm. (200 per cent) of hemoglobin, determined by the Sahli method. The patient was given sulfapyridine, and six days later the red cell count was 6,890,000, with 22.6 Gm. (156 per cent) of hemoglobin. Synchronously with this decrease of 3,000,000 red blood cells and the reduction in hemoglobin of 50 per cent, there appeared a precordial systolic murmur and enlargement of the left side of the heart. The heart measured 3.3 cm. from the midline to the right border and 17.6 cm. from the midline to the left border, with a total transverse diameter of 18 cm.

The patient was dismissed at the end of two weeks but was readmitted two months later for the same period, with recurrence of the pneumonia and the same findings as before. On April 25, 1942, at the age of 6 years and 5 months, she was rushed to the hospital because of the sudden onset of extreme cyanosis and

dyspnea. In spite of the administration of oxygen and stimulants, she lived only fifteen minutes.

Comment on the Clinical Diagnosis.—It was thought that there was either, or both, a patent foramen ovale or a patent ductus arteriosus because of the presence of the transient precordial systolic murmur. Although cyanosis was not present at birth, it developed when there was cause for obstruction of the respiratory tract,

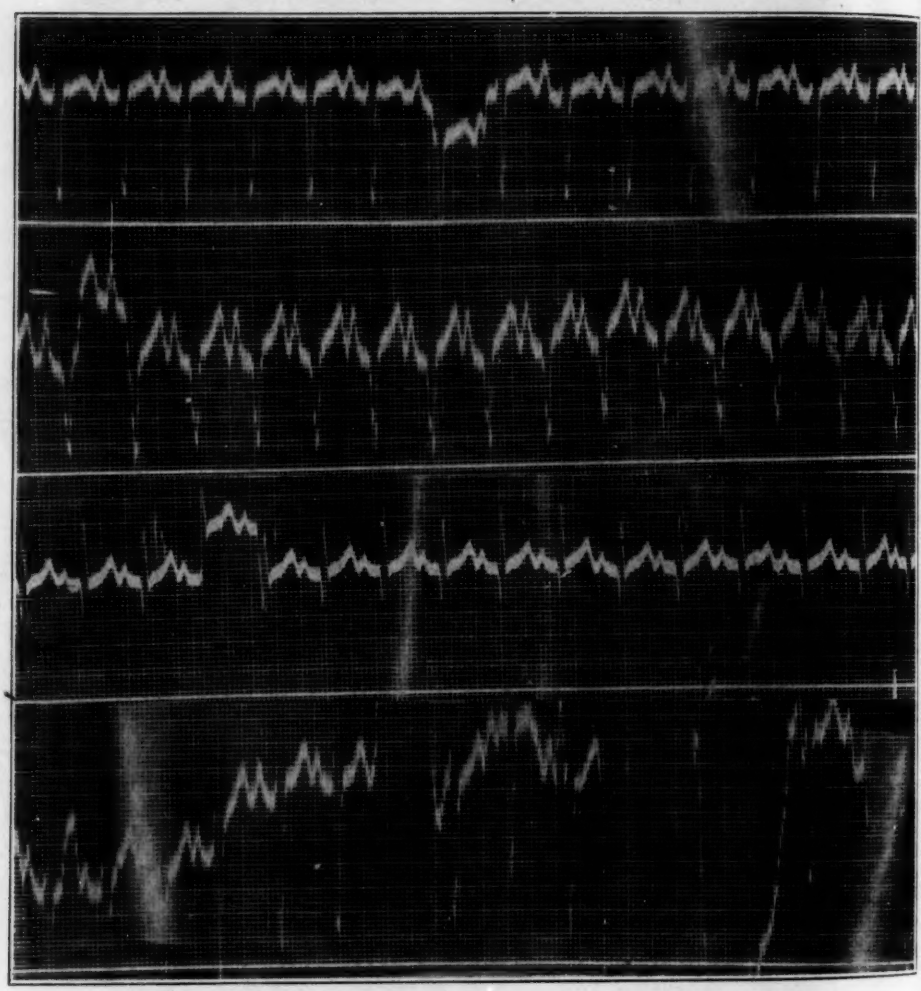

Fig. 2.—Electrocardiogram in a case of transposition of the great vessels.

which raised the pressure in the pulmonary circulation, causing temporary reversal of the flow of blood through the ductus (Lundsgaard's 1 factor), as discussed by Manhoff and Howe.[13] Roentgenograms, however, showed no widening of the pulmonary vessels, such as would be expected with a patent ductus arteriosus.

13. Manhoff, L. J., and Howe, J. S.: Am. Heart J. **29**:90-98, 1945.

The presence of the conspicuous venous pulse in the neck and the enlargement of the right side of the heart pointed to a patent foramen ovale, but on the roentgenogram what was interpreted as an aortic knob was not present as would be expected.

Transposition of the great vessels was suspected ante mortem. This anomaly, in which the aorta arises from the right ventricle and the pulmonary artery from the left ventricle, is rare. However, it was the only obvious way of accounting for the extreme cyanosis with the slight cardiac enlargement.

Autopsy Observations.—The heart and lungs with the great vessels weighed 500 Gm. The heart was globular and flattened. There was 25 cc. of clear, light straw-colored fluid in the pericardial sac. The left and the right ventricle were of about equal thickness, 10 to 12 mm.

There was transposition of the aorta and the pulmonary artery, so that blood from the right ventricle passed into the systemic circulation through a large vessel exactly similar to the aorta. The valvular opening just admitted the tip of the

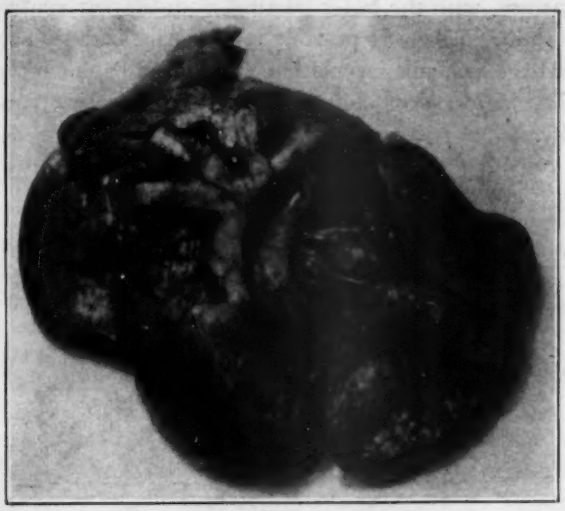

Fig. 3.—Heart and lungs, showing complete transposition of the great vessels.

little finger. A large and a small coronary vessel were given off at the base of the valve. The pulmonary artery passed from the left ventricle instead of the right ventricle. The pulmonary artery was broad at its base but narrowed to form the stems of the pulmonary arteries. The left auricle was small. There was a large patent foramen ovale between the two auricles. The two flaps of the foramen were superimposed for 2 cm., forming a competent valve.

Circulation.—Thus, venous blood entered the right auricle and passed through the patent foramen ovale to the left auricle, and thence to the pulmonary artery, lungs and right ventricle. Unaerated blood passed through the transposed aorta to the systemic circulation. The aerated blood returned from the lungs to the left auricle and passed through the pulmonary artery back to the lungs. However, a little aerated blood mixed with venous blood via the patent foramen ovale and thus reached the systemic circulation.

SUMMARY

The clinical features and postmortem observations in the case of a 6 year old child with congenital transposition of the aorta and pulmonary artery are described.

Symptomatically there were dyspnea, cyanosis (developing after birth), pulmonary osteoarthropathy, inability to gain weight, underdevelopment, prominent pulsations in the neck, slight enlargement of the right and left sides of the heart, polycythemia and absence of murmurs except for a transient systolic precordial murmur, coinciding with a decided drop in the erythrocyte count. Diagnosis was not aided either by roentgenographic examination of the chest or by the electrocardiograms.

The pathologic anomaly was transposition of the aorta and the pulmonary artery, with the latter passing from the left ventricle instead of from the right. Life was possible temporarily because some aerated blood reached the systemic circulation via a large patent foramen ovale.

The embryologic aspect of transposition of the great vessels is discussed briefly.

ACROCEPHALOSYNDACTYLY

H. GRAY, M.D., and L. B. DICKEY, M.D.
SAN FRANCISCO

AN UNEXPECTED number of requests for reprints of a recent paper on arachnodactyly (Gray[1]) reveals a sufficiently active interest in anomalies of the fingers to warrant reporting a patient with another rare variety of such an anomaly.

About half a century ago (1894) a case of congenital spoon-shaped hands, due to fusion of fingers, combined with peaked skull, was first reported by Wheaton.[2] The name was given to this condition by Apert[3] (1906). His clinical note was superficial, as indeed were most of the subsequent case histories in the rather scanty literature. The memoir of real authority is that by Park and Powers[4] (1920). Only 5 cases have appeared in the literature in this country, according to Sirkin,[5] while the total number of authenticated cases is about 80, according to Cohn.[6]

REPORT OF A CASE

This baby boy was born Sept. 24, 1944, of healthy parents and without any family history of congenital anomaly. At that time the mitten hands, sock feet, cleft palate, tower skull and parrot nose were evident. The anterior and posterior fontanels and the longitudinal suture were open. Exophthalmos was conspicuous. The nose was discharging mucopus. The palate was cleft, with a narrow opening, another anomaly not usually present in the syndrome as designated in the title. There was no harelip. The testes had descended into the scrotum. The heart, lungs and abdominal organs were normal, as were the results of laboratory tests.

The measurements taken at birth were: body length, 49.5 cm. (19.5 inches); weight, 3,540 Gm. (7 pounds 13 ounces); circumference of head, 34 cm.; circum-

From the Departments of Medicine and of Pediatrics, Stanford University School of Medicine.

1. Gray, H.: Arachnodactyly (Spider Fingers), Arch. Int. Med. **75**:215-221 (April) 1945.

2. Wheaton, S. W.: Two Specimens of Congenital Cranial Deformity in Infants Associated with Fusion of Fingers and Toes, Tr. Path. Soc. London. **45**: 238, 1894.

3. Apert, E.: De l'acrocéphalosyndactylie, Bull. et mém. Soc. méd. d. hôp. de Paris **23**:1310-1330 (Dec. 21) 1906.

4. Park, E. A., and Powers, G. F.: Acrocephaly and Scaphocephaly with Symmetrically Distributed Malformations of the Extremities: So-Called Acrocephalosyndactylism, Am. J. Dis. Child. **20**:235-315 (Oct.) 1920.

5. Sirkin, J.: Acrocephalosyndactylia: Report of a Case, Am. J. Ment. Deficiency **48**:335-338 (April) 1944.

6. Cohn, B. N. E.: True Oxycephaly with Syndactylism: Case Report, Am. J. Surg. **68**:93-99 (April) 1945.

ference of chest, 35 cm.; circumference of abdomen, 36 cm.; fontanel, 15 by 4 cm. At the age of 29 days, the weight was 3,289 Gm. (7 pounds 4 ounces); face length (mentum-nasion), 60 mm., and face breadth (bizygomatic), 88 mm. The head measurements are discussed later.

Roentgenographic Examination (Dr. Windholz; March 23, 1945).—This extraordinary case of acrocephalosyndactyly was characterized by a high vault, premature partial synostosis of the coronal suture and, apparently accessory, a partially open coronal suture, running through the middle of the parietal bone. The anterior fossa

Head Measurements

					Head					
					Length		Breadth		Auricular Height	
Observer	Date	Patient Normal	Sex	Age	Mm.	Ratio to Normal	Mm.	Ratio	Mm.	Ratio
Rieping, A.: Deutsche Ztschr. f. Chir. 148: 1-51 (Jan.) 1919	1919	Patient	F	New-born	80		60		95	
		normal			110		90		80	
						0.73		0.67		1.19
Park and Powers [4]	1920	D. H.	F	4 yr. 6 mo.	148		144		145	
		20 normal			174		138		127	
						0.85		1.04		1.14
Apert [3]	1906	P. G.	M	3 mo.	120		94			
		normal			133		109			
						0.90		0.86	...	....
deBruin, J.: Bull. Soc. de pédiat. de Paris 23: 399-414 (Sept. 26) 1925	1925	S. J. I.	F	3 mo.	120		115		110	
		normal			129		107		...	
						0.93		1.06		....
Bostock, J.: P. J. Australia 1: 572-574 (May 12) 1928	1928	M. S.	F	20 yr.	156		158		145	
		normal			190		146		126	
						0.82		1.09		1.15
		A. B.	F	12 yr.	172		161		151	
		normal			186		146		126	
						0.93		1.11		1.20
Bayssat, H.: Thesis, Paris, 1929	1929	S. R.	F	15 yr.	163		175		...	
		normal			186		146		126	
						0.88		1.20		....
Flinker, A.: Virchows Arch. f. path. Anat. 280: 546-553 (March 12) 1931	1931	J.	F	46 yr.	180		180 (1)		...	
		normal			190		146		126	
						0.95		1.24		....
Present case.....	1947	M.	M	29 days	114		102		115	
		normal			110		90		80	
						1.04		1.13		1.18
Averages.....						0.87		1.03		1.17

was short and flat; the middle fossa, extremely deep and probably twice or three times as large as normal. The posterior fossa was short, and the lambdoid and spheno-occipital sutures were open. Irregular translucencies (lacunas) were to be seen in the middle and posterior portions of the vault. Syndactyly was as previously described. There had been increase in bone age and in skeletal growth since the last examination, on September 29.

Psychometric Report (Feb. 9, 1945).—Results on the Gesell Developmental Schedules showed that at the chronologic age of 5 months, the approximate level of general development was 4 weeks plus and the approximate developmental quotient 20 plus. Because of the physical deformities of the baby, it was not possible to obtain a reliable developmental quotient. He could not, of course, grasp

Fig. 1 (Sept. 29, 1944).—Note tower skull, face and mittlike hands.

Fig. 2.—Roentgenogram of skull.

any object, and since the eyes did not converge it was difficult to determine whether he was able to follow objects, or even to see them. The nurses did not pull him to a sitting position in the crib, and this was not attempted. In the supine position, the head was in midposition and the arms were active. The hands did not engage in midline. In the prone position, there were crawling movements, the head was lifted to zone 11 recurrently and the legs were usually in a flexed position. The legs were greatly underdeveloped, and the feet were deformed, like the hands. The nurses reported that he appeared to reach for the bottle, but of course he could not grasp it. The baby's general development did not appear to be beyond the 4 week level, though the results of some tests in the motor field were at the 8 week level (i. e., lifting the head to zone 11 while in the prone position). The baby made only a few snorting sounds.

Summary: The patient was an extremely defective baby, whose developmental quotient was probably about 20. It was not possible to obtain a reliable test.

Head Measurements.—With the common clinical practice of noting only the circumference of the head one misses the enlightenment to be had from measuring

Fig. 3.—Roentgenogram of feet.

the length (from the glabella to the farthest point on the occiput), the breadth (maximum biparietal width) and height (the so-called auricular height, from the top of the ear hole). The evidence collected is presented in the table, in which the noteworthy feature is that on the average head breadth is to the standard as 1.03:1.00; i. e., only 3 per cent greater than normal; so it may be said not to be abnormal. But the head length is 13 per cent below normal; and, of especial note, the height is as much as 20 per cent over normal, averaging 17 per cent in excess. This proportion is characteristic of the so-called tower skull. In passing, it may be noted that the ratio of boys to girls listed in this table is only 2:7.

Pathologic Report (Dr. J. B. McNaught).—On March 19, 1945, the patient died, at the age of 176 days. At autopsy the body length was 62 cm. and the weight 3,380 Gm. The autopsy report was as follows: "The clinical diagnosis was acrocephalosyndactyly, cleft palate and bronchopneumonia. The anatomic observations were the congenital malformations, acrocephalosyndactyly and cleft palate; bronchopneumonia (cause of death), with acute bronchitis; decubital ulcer of the sacrum; subacute meningitis (cause unknown), and chronic ethmoidal sinusitis.

"Weights of organs: The thymus weighed 5 Gm.; the spleen, 8 Gm.; the heart, 25 Gm.; each kidney, 25 Gm.; each lung, 50 Gm.; the liver, 120 Gm., and the brain, 680 Gm. Except for patchy bronchopneumonia, all the organs appeared normal, as did the gastrointestinal tract, pancreas, adrenal glands and vertebral marrow. Histologic examination revealed nothing notable except for pus in the lungs and hyperemia of the kidneys."

All in all, the appearance of this patient was more typical than individual, as is common among children with developmental anomalies of bone such as cretinism and spider fingers (arachnodactyly). This nosologic type is most easily visualized by photographs (figs. 1 to 3).

PROGNOSIS

In patients with as extensive defects as those in the present case, the outlook is bad. But when deformity is confined to synostosis of the cranial sutures, hope exists provided every physician seeing an infant is on the watch for the peculiar-shaped head, differentiates the synostosis early and can obtain a competent neurosurgeon to excise strips of bone, preferably before the age of 6 months (Faber and Towne [7]).

SUMMARY

A case of acrocephalosyndactyly, combined with cleft palate, parrot nose (psittacorhinia) and exophthalmos, is reported, with head measurements.

Stanford University Hospital.

---

7. Faber, H. K., and Towne, E. B.: Early Operation in Premature Cranial Synostosis for the Prevention of Blindness and Other Sequelae, J. Pediat. **22**:286-307 (March) 1943.

Progress in Pediatrics

NATURE AND TREATMENT OF STUTTERING

PHILIP J. GLASNER, B.C.S.
BALTIMORE

THE PROBLEM of stuttering has been treated in the past, and is still frequently treated, with a nonchalance unjustified by the effects it so often produces on the person afflicted with this disorder. Many physicians tend to regard stuttering as a temporary phenomenon, usually outgrown, and, therefore, a condition to be ignored. Unfortunately, the same physician does not usually follow a child through adolescence to adulthood and is unable to observe the seriousness of such a prognosis. It is true that there are many children who, diagnosed as stutterers by their parents, cease to show this symptom after a time. This does not mean that the child outgrew the condition but that changes took place within the child or in his environment which were conducive to the development of normal speech. As a matter of fact, numerous surveys show that there is the same incidence of stutterers at the freshman level of college as in the third grade.[1]

Stuttering has its essential origin in early childhood, usually between the ages of 2 and 4, and is a manifestation of some emotional disturbance. Unless the pediatrician or attending physician becomes familiar with the causes and the nature of stuttering, it will be impossible to reduce the incidence of this condition, which afflicts approximately 1 per cent of the population.[2] When treatment is initiated in early childhood, soon after the symptom is observed by the parent, the condition usually disappears without the patient's ever being conscious of the problem. As a child grows older, his speech habits become established, and it is rare, therefore, for a child suddenly to begin to stutter after the age of 7. When this does occur, it is usually on a hysterical basis or is caused by some strong traumatic experience, which can be corrected by sedatives and psychiatric consultations.

In the past twenty years, many valuable data have been accumulated in psychiatric clinics and university laboratories. Contrary to earlier beliefs, it has been found that the causes of stuttering are of a functional or psychogenic nature rather than of physical origin. From the

From the Children's Psychiatric Service, Johns Hopkins Hospital.

1. Bender, J. F.: The Personality Structure of Stuttering, New York, Pittman Publishing Corporation, 1939, table 1, p. 2.

2. Bender,[1] table 2, p. 2.

days of the ancient Greeks to the latter part of the nineteenth century, the focus of attention was on the peripheral organs of speech. As late as 1850, there were physicians in Germany, England, France and the United States who were cutting wedges in the tongue as a form of treatment. Until recently many scientists held that the condition was the result of a conflict between the two cerebral hemispheres, in which a left-handed person trained or forced to use his right hand was unable to establish a dominant gradient. Recent evidence has not substantiated the theory of cerebral dominance,[3] and the emotional involvements in cases of stuttering have been recognized. Thorough physical examinations and laboratory studies have failed to reveal evidence of constitutional inferiority or organic disease in stutterers.[4]

Variations in the symptoms of stuttering are so numerous that they are confusing to lay and professional persons alike. Parents seeking advice and treatment for an apparent abnormality in a child's speech often give evidence of this in voicing the complaint in such language as, "He hesitates in his speech," or "He doesn't stutter, but he just can't get the words out," or "His words get caught in his throat," or "When he tries to talk he can't catch his breath." The manifestations are so diverse that it is safe to say that no two stutterers stutter alike.

In order to understand the problem, it is necessary to understand the development of stuttering. When a child deviates from the speech standards established by society, particularly in the rhythm of speech, he usually does not do it intentionally, nor does he regard his deviation as a problem. He speaks to the best of his ability, his speech usually reflecting his emotional and physical status. When the deviation is of a repetitive nature, the repetition in most cases is merely a reflection of the child's personality makeup. At an early age, when the repetition is of an effortless nature, it should not be regarded as an indication of stuttering. Since speech is a learned process and speech habits usually are not established until a child is approximately 8 years of age, it is obvious that any unfavorable condition can inhibit the flow of speech so as to create a break in rhythm. Adults frequently repeat syllables and words or find it difficult to initiate a sound when they are lost for words, confused, excited, nervous, surprised, tired, frightened, anxious or otherwise thrown off their stride. It is easy, therefore, to see how these same factors would momentarily affect the speech of a child, whose speech habits are not yet conditioned. An adult recognizes his speech behavior during moments of tension as the result of an unusual experience and accepts his speech conduct as normal for

3. Johnson, W.: A Study of the Onset and Development of Stuttering, J. Speech Disorders **7**:251-257 (Sept.) 1942.

4. Meyer, B. C.: Psychosomatic Aspects of Stuttering, J. Nerv. & Ment. Dis. **101**:127-157 (Feb.) 1945.

the situation; he does not interpret it as a sudden indication of stuttering. Similarly, speech hesitancies due to such experiences should not be considered evidence of stuttering in children. Frequent exposure to experiences which inhibit a child's fluency will, however, tend to weaken the speech pattern which is in the process of being developed. Repetition of sounds and words is common to all children. It has been estimated that some normal children repeat as many as one out of every five words during the early stages of their speech development.[5] At this point in development the child is comparatively relaxed and shows no evidence of tension. This relaxed, effortless repetition and hesitation should not be regarded as stuttering. Parents who are overprotective and overanxious, or who are annoyed with this type of speech, may criticize or correct the child's manner of speaking in such a way as to make him feel he is doing something abnormal or strange. It would be natural for an intelligent, sensitive child to react to this criticism with bewilderment and feelings of inferiority, thus creating tension. There is a difference in the type of hesitations and repetitions normally produced by children and those produced when a child is tense and emotionally involved. When the child is under tension, his speech is characterized by a change in muscle tonus, pitch, speed and rhythm. The hesitations or blocks are forced and are of longer duration, and the repetitions are more strained and obvious.

Any condition or situation which can produce disturbances of a behavioral or emotional nature in children may precipitate the kind of speech that is referred to as stuttering. As a rule the causative factors in each case are multiple rather than singular and occasionally are difficult to determine. However, after examination and study of many children who were regarded as stutterers by their parents, it has been possible to determine the specific conditions which may create feelings of tension, unrest and insecurity within a particular child. These factors may be listed as follows:

1. Overstimulation or pampering, particularly in homes in which more than the usual two adults are present. This condition usually exists when grandparents or maiden aunts live in the same house. The relatives may want to play with the child when he should be resting, or they may countermand requests of or discipline imposed by the parents or inject criticisms of their own. In such an environment it is impossible for a child to relax.

2. Overconcern about eating on the part of the parents, which may border on or result in coercion. Many mothers place excessive

5. Davis, D. M.: The Relation of Repetitions in Speech of Young Children to Certain Measures of Language Maturity and Situational Factors, J. Speech Disorders **4**:303-318 (Dec.) 1939.

emphasis on the importance of diet and seriously believe that if the child does not consume the required amount of vitamins at each meal illness is sure to follow. As a result, a battle between mother and child frequently ensues.

3. Inhibition of the freedom and relaxation essential to the child's well-being by an overprotective mother. The mother who continuously watches, follows, and hovers over a child with such remarks as "Don't touch that," "Watch out," "Don't do that," or "Be careful," creates a tremendous amount of inhibition, which may reveal itself in the child's speech.

4. Inconsistency of treatment by the mother and by the father. During the day the mother allows the child the freedom of the house. He is permitted to run and play in his own way, but when his father comes home everything must immediately change. Because his father is "too tired," the child cannot run; he cannot yell, and he cannot expect any understanding or affection from his father. This can become confusing and disturbing to a child.

5. Hasty diagnosis on the part of the parents in cases in which there is a history of stuttering in the family or in which either parent is aware of the problem of stuttering. In such cases, the normal repetitions and hesitancies discussed earlier are immediately interpreted as stuttering. To a parent who stutters, or to one who has a stuttering sister or brother, any indication of stuttering on the part of the child spells calamity. Stuttering parents have been known to consult physicians regarding the possibility of the trait being inherited. Some persons refrain from having children in the fear that their offspring will also stutter. It can be understood why these parents can so easily become disturbed over any deviation in speech of their children.

6. Feelings of insecurity based on quarreling between the parents or on impending divorce. An example is the case of a 13 year old boy with a history of stuttering for nine years who had been living in constant dread of his parents' separation. At the age of 4, he had been told that his parents intended to separate; although this never happened, they quarreled constantly. Meanwhile two aunts had obtained divorces, and he was fearful that his parents would follow the family pattern. During the first visit to the clinic the patient was able for the first time to express his fears to the therapeutist, thus relieving himself of much of his tension. The parents were informed of the effect their marital difficulties had on their son, and they were able to reconcile many of their differences. The patient was also given treatment on a symptomatic basis, and after the third visit the stuttering was no longer evident.

7. Insecurity based on frequent changes of residence. This feeling usually occurs in cases in which the father's occupation necessitates fre-

quent moves from one section of the country to another. The readjustment to new homes, playmates and schools, sometimes as often as three or four times a year, tends to the development of feelings of insecurity.

8. Differences in speech development. Since speech is a learned process, there will necessarily be individual differences in its acquisition. Some children progress more rapidly than others. Impatient or uninformed parents will frequently correct a child for errors in articulation, pronunciation and grammatical construction to the point that the child becomes confused and is tense whenever speech is required.

9. Feelings of insecurity produced in an older child by improper handling after the birth of a sibling. The first child was formerly the focus of all attention and was permitted to do as he pleased; but with the new baby's arrival he abruptly becomes the "big brother" and is expected suddenly to behave as such.

10. Sibling rivalry is a frequent cause of emotional stress and tension within a child. Parents who do not appreciate or understand the individual differences among children will frequently compare the intelligence, social attainment, appearance, motivation and other characteristics of one child with those of a sibling. Whether openly expressed or merely implied, such comparisons create a conflict within the child.

There are other psychologic and environmental factors of an inhibitory and disturbing nature which also have an unfavorable effect on a child's speech. However, when the causes are determined in early childhood and the irritating conditions remedied, the disorder soon disappears, without recurrence.

It is interesting to note that stuttering has not been found among Indians on the reservations,[6] where the customs are different, particularly in regard to child care and child training. Moreover, many anthropologists studying the culture and customs of primitive tribes have reported that stuttering is not known among them,[7] whereas the incidence of stutterers among all civilized people with similar cultures is approximately 1 per cent. These observations, of course, are additional evidence that stuttering has an environmental and a psychologic basis rather than a physical basis.

Stuttering, unlike many other disorders of childhood becomes progressively worse as time goes on if the causes are not removed. At the onset there may be periods when the child is free of all symptoms. His behavior may not at first be outwardly affected. His symptoms

6. Johnson, W.: The Indians Have No Word for It: I. Stuttering in Children, Quart. J. Speech **30**:330-337 (Oct.) 1944.

7. Bullen, A. K.: A Cross Cultural Approach to the Problem of Stuttering, Child Development **16**:1-88 (March-June) 1945.

are not unduly exaggerated. Up to the point where he does not have a fear reaction to speech, he should be considered not as a stutterer, but as a potential stutterer. Sooner or later, however, when parents, or society at large, place a stigma on his speech, he becomes apprehensive in situations where the penalty or the embarrassment is the greatest. There develops a feeling of expectancy to stuttering, and he will invariably stutter again in those situations. He sems to acquire a "conditioned response." When he is confronted with a stimulus which has previously been disturbing, such as asking a stranger a question, reciting before certain teachers, voicing an opinion before a group of people or speaking to an impatient parent, he responds again with the same difficulty in speech. Although the past experiences frequently are not on a conscious level, he nevertheless seems involuntarily to be overcome by an expectancy of stuttering. Stuttering becomes a serious problem when the person labels himself as a stutterer and develops a fear of stuttering. Then it becomes not only a speech disorder but a neurotic manifestation as well. The stutterer begins by fearing a few situations and certain people, but as his unsatisfactory experiences multiply, his area of fear becomes broader. Along with his fear of stuttering, he experiences strong anxiety feelings, such as severe palpitation, trembling of the limbs, excessive perspiration, pains in the chest, tightening of the muscles of the stomach or choking sensations, whenever he thinks he may stutter. His outward behavior usually changes as time goes on. He withdraws from many activities in which he formerly participated. He may avoid oral reading and recitation at school. He may avoid social functions that were pleasurable in the past. He may refuse to go to the store unless given a note with the desired items. His disposition also frequently changes, and he becomes irritable, moody and generally unhappy. Besides the emotional and personality changes involved, the problem may also have an effect on the person's attitude toward school and vocation. Because of their attitude toward their speech, some stutterers find the struggle of social contact and communication at school so difficult that they withdraw from it much sooner than their intellectual ability warrants. It is common for these persons not to direct their energies into the vocational field for which they are best fitted, but to choose an occupation which requires little speech.

As the patient becomes involved in his problem, the pattern of stuttering undergoes many changes. In his attempt to avoid speaking in the unacceptable manner, he may substitute mannerisms which to him at the moment are a relief from his condemned speech. He may acquire tonic and clonic spasms of the speech musculature. Bodily movements, gritting of the teeth, blinking of the eyes, head shaking, facial grimaces, gasping movements and stamping of the feet are further developments of the original symptom and are only some of the many

devices to which he may resort in order to break the stuttering block. The average stutterer becomes rather proficient in the use of synonyms. When he finds it difficult to utter a particular word, he tries to find a substitute, even though it may not convey the desired thought. Some stutterers become so adept at camouflaging their speech that their friends and relatives believe they have overcome their defect. The stutterer does not find this an acceptable adjustment, since his impromptu choice is not always a satisfactory substitute and he is never confident that he will have a synonym at hand. Since no two stutterers stutter alike, each acquires his own set of symptoms and mannerisms, depending on the movements which he finds expedient.

Treatment should be based on the results of a careful examination, which takes into consideration such factors as causes, age, personality, present environment, attitudes, emotional problems and, of course, symptoms. The therapeutist should never think in terms of treating stuttering, but should treat the personality as a whole. Therefore, the treatment should always be on an individual basis. When the disorder occurs in early childhood, the causative factors are of prime importance, and the child should never be made to feel that he "stutterers" or is abnormal in any way. At this period, if the family is cooperative, only a few visits are necessary. Sometimes one or two consultations can remove the source of the difficulty. When the child is aware of his condition, but has not formed a stuttering personality, it is necessary to apply psychotherapeutic technics to relieve the tension and to help him gain a feeling of security. The therapeutist should develop an intimate relationship with the child, giving him as much understanding, approval, acceptance and support as are necessary. Stuttering, as such, must never be discussed with the child. Whenever symptomatic treatment is indicated, it is given in a simple, casual manner at the child's level of understanding. The environment should always be taken into consideration, and the parents should be seen regularly, so that the sources of irritation can be removed.

The following case is illustrative.

John E., a boy aged 2 years 7 months, was referred to the clinic by his pediatrician because of "marked stuttering." He was in good physical health, and the only other complaint was nocturnal bed wetting. He began to talk at 11 months and spoke in sentences at 18 months of age. When stuttering was first noticed, at the age of 2 years and 3 months, the advice of the pediatrician was to ignore it. The problem was never discussed in the child's presence. Two months later the stuttering was so pronounced that when blocking occurred the patient would cry and declare, "I can't talk." He frequently refrained from speaking, and changes in personality became noticeable. He became moody and difficult to manage. His voice became higher in pitch, which caused his father to report that it reminded him of a deaf child he knew.

John and his parents lived with the maternal grandparents in a six room house. Mrs. E. was an only child. Mr. E. was a kind, but overanxious, father, who took his fatherhood seriously. The maternal grandmother was on the "nervous side." The patient formed a close attachment to his easy-going maternal grandfather. His parents and grandparents were proud of John's early ability to recite and sing and frequently pressed him to perform. The constant presence of adults resulted in his failure to develop the ability to occupy himself, nor did he at any time desire to be alone. In this setting there was little opportunity for relaxation.

After a few visits the stuttering decreased, and at the seventh visit the patient was entirely free from symptoms. His behavior returned to that of a pleasant, happy child, and the bed wetting soon ceased. There were no relapses. John is now 7 years old and has shown no further evidence of stuttering.

In the case of an older child, adolescent or adult whose stuttering has continued for many years and in whom emotional and personality complications have developed, determination and treatment of the cause or causes will not as a rule remedy the speech disorder. The stutterer accumulates mass of speech experiences and associations which obliterates the original causes of his difficulty and accentuates the symptoms. It is necessary, therefore, for an older patient to have an understanding of the nature and causes of stuttering in order that he may have a correct orientation toward his problem. The patient's attitude toward himself and his speech must be adjusted before any symptomatic treatment can be successful. The average stutterer is constantly haunted by the dread of stuttering because he is overconcerned with the impressions and reactions of his listener. The stutterer must be helped to develop a sense of objectivity. When he learns to accept himself as an individual, with many assets and some liabilities, he will be able to live a normal life, without overemphasizing the importance of his stuttering speech. The patient should also have an opportunity to work out his other mental and physical problems, so that he may be relieved of as much tension as possible. Unless the patient can also obtain symptomatic relief, the psychotherapeutic results will usually be temporary. Symptomatically, the patient is informed that his goal is not to cure his speech, but to learn how to control it. He is taught to recognize the fact that in speaking every one blocks and repeats at times. The reeducational speech program is based on the development and establishment of a normal, relaxed speech pattern that the patient can control. This pattern is worked out step by step, with the therapeutist first attacking the most obvious symptoms, pointing out the mistakes and then teaching the patient the proper controls.

Since stuttering can have such far reaching effects on the emotional, social, educational and vocational life of a person, it is imperative that treatment be initiated as soon as it is indicated.

Children's Psychiatric Service, Johns Hopkins Hospital.

News and Comment

GENERAL NEWS

***Pediatrics*, Published by The American Academy of Pediatrics.**—The American Academy of Pediatrics has announced the inauguration of a new journal to be called *Pediatrics*. It will be owned, edited and controlled by the Academy. Charles C Thomas, Publisher, of Springfield, Ill., will be the publisher. Dr. Hugh McCulloch, St. Louis, will be editor in chief. The editorial board will consist of Dr. C. Anderson Aldrich, Rochester, Minn.; Dr. Allan M. Butler, Boston; Dr. Harold K. Faber, San Francisco; Dr. Arild E. Hansen, Galveston, Texas; Dr. Rustin McIntosh, New York; Dr. Irvine McQuarrie, Minneapolis; Dr. Edwards A. Park, Baltimore; Dr. Grover F. Powers, New Haven, Conn., and Dr. Joseph Stokes Jr., Philadelphia.

The first issue of the new journal will appear early in January 1948, and monthly thereafter. The name *Pediatrics* has been chosen to indicate the wide interest of the specialty of pediatrics. Besides the original articles on clinical pediatrics, there will be papers in the related fields of nutrition, genetics, public health and preventive medicine, psychology, nursing and medical sociology, education and social welfare of children. Persons submitting original articles need not be fellows of the Academy. Proceedings and reports of national interest from the Academy will be included. Sections on subjects related to pediatrics as submitted by contributing editors will appear at intervals. The scope of *Pediatrics* will be international, with a special section devoted to Latin-American countries, where the Academy already has a program in operation. This program includes close cooperation with universities, pediatric hospitals and centers and pediatric societies in those countries. Abstracts of all original articles will be published in Spanish.

Special effort will be made to report objectively matters of interest occurring in the Conogress and in the government departments and agencies in Washington, D. C. *Pediatrics* will also be used as a medium for reports from the study of child health services being conducted by the Academy in cooperation with other national, state and local agencies. *Pediatrics* will represent the Academy and will also interpret pediatrics as a special practice of medicine in the broad field of child welfare and diseases of children through research, clinical practice and education.

All communications of an editorial nature should be addressed to the editor in chief, Hugh McCulloch, M.D., 325 North Euclid Avenue, St. Louis 8. Advertising, business matters and subscriptions should be sent to Charles C Thomas, Publisher, 301-327 East Lawrence Avenue, Springfield, Ill.

Medical Publications Needed Overseas.—As a result of war and persecution, doctors, dentists and technicians in allied fields throughout Europe have been deprived for more than ten years of news of the latest developments in their professions—the kind of news and analysis contained in this journal.

When you have finished with this issue, put it to work by sending it to the SOS (Supplies for Overseas Survivors) Collection of the Joint Distribution Committee, 1539 Troy Avenue, Vanderveer Park, Brooklyn. It will be placed in a library in a D. P. camp, child care center, hospital or school, for use by professional men and women desperately anxious to bring themselves up to date on the knowledge forcibly kept from them by the Nazis.

Obituaries

DANIEL LESESNE SMITH, M.D.

1877-1947

Daniel LeSesne Smith died in Mission Hospital, Asheville, N. C., on July 7, 1947, three weeks before his seventieth birthday. He was born at Hell Hole Swamp, Berkeley County, S. C., on July 28, 1877, moved to Hungry Neck, Mount Pleasant, S. C., in 1886 and here spent his early childhood. Later he attended high school at Charleston, received his degree of Bachelor of Arts at Clemson College in 1901 and graduated from the Medical College of the State of South Carolina in Charleston, S. C., in 1903. After six years of general practice at Newry and Great Falls, S. C., he moved to Spartanburg, where his practice was limited to pediatrics after 1914. He soon established the Infants and Children's Sanitarium and the Spartanburg Baby Hospital at Saluda, N. C. Here, also he and Dr. Frank Howard Richardson organized the Southern Pediatric Seminar in 1921, which has since been a powerful force in postgraduate pediatric education. The course was planned especially to fit the needs of the general practitioner and has been attended by nearly 2,000 practicing physicians from the South.

Dr. Smith was a member of many medical and scientific societies, in whose work he took an active interest. As president of the South Carolina Medical Association in 1927, and as chairman of the pediatrics section of the Southern Medical Association in 1932, he served with distinction. In some respects he was many years ahead of his generation. Having appreciated early the great need for better training of the general practitioner of medicine, who takes care of the large majority of the children in this country, he devoted much of his time to the attainment of better facilities for pediatric teaching in the South. He was a charter member of the American Academy of Pediatrics and had served since 1930 as one of the board of directors of the South Carolina Sanatorium, State Park, for tuberculosis. He was elected to the South Carolina State Board of Health in 1930 and was attending physician at Cedar Springs for Blind, Deaf and Dumb Children since 1914.

In 1904 he married Ammie Hane; to them were born 4 children: Daniel LeSesne Jr., Keitt Hane Smith, Samuel Porcher Smith and Nettie Hane Smith. Ammie Hane Smith died in 1911, and in 1913 he married Nettie Hane, sister of Ammie. Two of the sons who survive him are engaged in the practice of medicine: LeSesne Jr., of Spartanburg, S. C., is a pediatrician, and Keitt, of Greenville, S. C., is a urologist.

Such is the biographic record of a man who was beloved and respected in his chosen field. He made an enviable place for himself in pediatrics and in American medicine. He did a great deal in his community and state to improve medical conditions for children and was a pioneer in child health work.

Many will remember him for his varied interests and loyal friendships. He loved fishing and always had a fund of appropriate stories or anecdotes to relate. In the passing of LeSesne Smith pediatrics has lost one of its great characters. Those who knew him best feel that they have been greatly enriched by the privilege.

WARREN W. QUILLIAN, M.D.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

FURTHER STUDIES ON THE CALCIUM REQUIREMENT OF PRESCHOOL CHILDREN. DOROTHY SHELDON MCLEAN, GLADYS KINSMAN LEWIS, ELIZABETH JENSEN, MILICENT HATHAWAY, HERTA BREITER and JULIA OUTHOUSE HOLMES, J. Nutrition **31**:127 (Jan.) 1946.

Assuming that children, under acceptable dietary conditions, can secure approximately 300 mg. of calcium daily from the nonmilk foods which they eat and that such calcium is utilized to the same extent as that of milk, the requirements of 6 of the preschool children studied by McLean and her associates would have been met by a milk supplement no greater than 2 cupsful. One child would have needed as much as ¾ quart (750 cc.).

FREDEEN, Kansas City, Mo.

STUDIES OF THE NUTRITIVE VALUE OF FISH PROTEINS: I. EVALUATION BY THE RAT GROWTH METHOD AND BY THE CANNON METHOD. HARRY J. DEUEL JR., M. C. HRUBETZ, CORNELIA H. JOHNSTON, RICHARD J. WINZLER, ERNEST GEIGER and G. SCHNAKENBERG, J. Nutrition **31**:175 (Feb.) 1946.

The authors report that the mixed proteins of mackerel, sardine and tuna muscle afforded superior growth to that with casein in weanling rats when fed at levels which gave suboptimal growth with casein. Mackerel protein was superior in that it caused greater recovery in weight and more pronounced stimulation in regeneration of hemoglobin, while possessing a potency equal to that of casein in the regeneration of plasma protein.

FREDEEN, Kansas City, Mo.

STUDIES OF THE NUTRITIVE VALUE OF FISH PROTEINS: II. THE USE OF MACKEREL PROTEIN IN THE BIOASSAY TEST FOR VITAMIN A. HARRY J. DEUEL JR., M. C. HRUBETZ, CORNELIA H. JOHNSTON, HILDA S. ROLLMAN and ERNEST GEIGER, J. Nutrition **31**:187 (Feb.) 1946.

The authors have demonstrated that a commercially prepared mackerel protein powder is satisfactory for use in bioassay experiments for the determination of vitamin A. When uniform doses of vitamin A were administered daily, greater growth was obtained in rats receiving the fish protein diet than in litter mates fed the corresponding casein diet. It is suggested that greater growth may result with limited amounts of vitamin A when a protein of higher nutritive value than casein is administered.

FREDEEN, Kansas City, Mo.

EXPERIMENTAL RESEARCHES ON THE VITALITY OF HUMAN MILK IN RELATION TO THE PERIOD OF NURSING. E. PICCARDI and E. MESSERI, Riv. di clin. pediat. **44**:160 (March) 1946.

It has been proved experimentally that a longer or shorter period of lactation has no influence on the vitality of milk. This interesting fact is framed within the biologic problem of how long breast feeding should last.

AUTHORS' SUMMARY.

ACUTE DEHYDRATION IN THE INFANT; CONTRIBUTION TO ITS PATHOGENESIS; ORIGINAL MODEL OF NEEDLE; A NEW SUBSTITUTE FOR HUMAN PLASMA: "DISANAPHYLACTIZED" CALF SERUM. R. RAMOS and W. OPPENHEIMER, Rev. españ. de pediat. **2**:162 (March-April) 1945.

The first part of this article is devoted to a discussion of the physiology of alimentary toxicosis and shock, giving the rationale for plasma transfusion for

infants with this condition. Levels of total circulating blood and plasma were low in the majority of the patients tested. Intravenous administration of plasma is felt by the authors to be most useful in the treatment of these infants. A detailed technical discussion of method is then given, the authors favoring the use of scalp veins.

On account of the difficulty of obtaining sufficient human plasma, Masson's plasma was used. This is the plasma of a calf diluted with water and heated to 100 C. with formaldehyde and ammonia. The resulting liquid is not coagulated by heat and has lost its clotting properties and protective antibodies. While weakly antigenic in itself, it precipitates wth serum prepared by immunizing guinea pigs against unaltered calf serum. By using this precipitin test on serum of babies given transfusion, it was found to be eliminated from the circulation slowly. Transfusion of 54,330 cc. into a large unstated number of infants and children was made without untoward reaction and with excellent clinical results.

If these results are verified and confirmed, it seems probable that Masson's plasma will have a great field of usefulness.

MILLER, Newark, Ohio.

NOURISHMENT OF INFANTS WITH MARES' AND ASSES' MILK. E. FREUDENBERG, Ann. pædiat. **166**:338 (June) 1946.

The feeding of mares' and asses' milk to infants is discussed as far as reports could be traced in the literature. Further, the results of chemical analyses of mares' milk are reported, which can be shown to be an albumin milk, containing comparatively little protein, little fat, but much lactose. The calorific value is low. Estimation is made of vitamins A, B_1, B_2, B_6, C and D. Genuine mares' milk cannot be used for feeding purposes without the addition of 1 to 1.5 per cent cows' milk fat. The fate of protein, fat, calcium and phosphorus in 3 children fed on this formula was investigated, and the results are reported. The urine was investigated, special attention being paid to the acid-base balance, which led to problems requiring further investigation. The feces were examined for their p_H, proportion and titrimetric acidity of fat, contents of ash, sodium and calcium, as well as bacterioscopically, Gram stain being used.

AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

THE ROLE OF THE CO-ENZYMES OF THE B COMPLEX VITAMINS AND AMINO ACIDS IN MUSCLE METABOLISM AND BALANCED NUTRITION. SIMON L. RUSKIN, Am. J. Digest. Dis. **13**:110 (April) 1946.

The vitamins of the B complex are ineffective in a diet when the proper amounts of all the amino acids and adenylic acid are not included. Adequate amounts of these three are essential to form the respiratory enzymes from which is derived the necessary energy for muscular contraction.

The chemistry of muscular contraction is discussed. The injection of the iron salt of adenylic acid ("irony," 34 mg.) causes relief from muscular fatigue; it also relieves coronary spasm.

The essential amino acids in the various foodstuffs are tabulated. Yeast, lactalbumin and whole egg are considered 100 per cent biologic in that they possess the essential amino acids in proper balance. A larger caloric intake is necessary to obtain the amino acids in sufficient amounts when the grain and vegetable proteins are used. This point is important when a starving people is being fed.

A hydrolysate protein is more easily assimilated in infants and the aged. The expense and difficulties of preparation are discussed. An enzymatic hydrolysis offers the best opportunity for retaining the full biologic value of a protein. It is stated that the yeast hydrolysates are the more palatable.

KIMBALL, Evanston, Ill.

THE THIAMINE, RIBOFLAVIN, NICOTINIC ACID AND PANTOTHENIC ACID CONTENT OF COLOSTRUM AND MILK OF THE COW AND EWE. P. B. PEARSON and A. L. DARNELL, J. Nutrition **31**:51 (Jan.) 1946.

Pearson and Darnell found a definite species difference in the amounts of thiamine, riboflavin and nicotinic acid in both the colostrum and the milk of the cow and the ewe. The latter's milk and colostrum were much richer in these vitamins. The colostrum of both the cow and the ewe was much higher in thiamine and riboflavin than was the milk. There was no significant difference in the nicotinic acid content of cow's colostrum and that of the milk, but ewe's milk contained almost twice as much as the colostrum. The pantothenic acid level of the milk of both species was higher than that of the colostrum.

FREDEEN, Kansas City, Mo.

THE RELATION OF VITAMIN A INTAKE TO LENGTH OF LIFE, GROWTH, TOOTH STRUCTURE AND EYE CONDITION. HENRY E. PAUL and MARY F. PAUL, J. Nutrition **31**:67 (Jan.) 1946.

The Pauls, in their study of albino rats on a vitamin A–free diet, found that the life span increased with increasing vitamin A intake, at levels of 1, 2, 4 and 20 U. S. P. units of vitamin A per hundred grams of body weight. They found that the effect of increasing vitamin A levels was similarly reflected in the four physiologic criteria studied—life span, growth, tooth structure and ocular condition. From their study, the vitamin A requirement of the albino rat, estimated on the basis of maximum life span and optimal growth, may be approximated at 10 U.S.P. units of vitamin A per hundred grams of body weight.

FREDEEN, Kansas City, Mo.

THE RELATION OF THE AMOUNT OF THIAMINE IN THE RATION OF THE HOG TO THE THIAMINE AND RIBOFLAVIN CONTENT OF THE TISSUE. W. W. HEINEMANN, M. E. ENSMINGER, T. J. CUNHA and E. C. MCCULLOCH, J. Nutrition **31**:107 (Jan.) 1946.

A positive relationship was found to exist between the thiamine intake and the deposition of this vitamin in the tissues of the hog. Thus, according to the authors, it may be possible to increase the content of thiamine in pork by using feeds with a high concentration of this vitamin. A thiamine deficiency had no lowering effect on the deposition of riboflavin in the skeletal muscle tissues, but there was a slight increase in the concentration of riboflavin in the liver and heart. Data obtained showed that storage of thiamine occurred and that the hog could utilize stored thiamine over a long period.

FREDEEN, Kansas City, Mo.

VITAMIN C CONTENT OF MARKET MILK, EVAPORATED MILK, AND POWDERED WHOLE MILK. AUBREY P. STEWART JR. and PAUL F. SHARP, J. Nutrition **31**:161 (Feb.) 1946.

The authors found that fresh powdered whole milk averaged 12.5 mg. of vitamin C per liter when reconstituted, as compared with 5.8 mg. for market milk and 2.0 mg. for evaporated milk, showing that the powdered whole milk was capable of contributing an appreciable amount of vitamin C to the diet. The stability of vitamin C in powdered whole milk, even on long storage, made this product a good source of the vitamin.

FREDEEN, Kansas City, Mo.

THE CAROTENE CONTENT OF CUBAN FOODS. JUAN J. ANGULO, CESAR FUENTES and MARGARITA JOHNSON, J. Nutrition **31**:463 (April) 1946.

The investigators determined by the chromatographic technic of Wall and Kelley the carotene content of 75 samples of 43 Cuban plant foods. In general, Cuban fruits were richer in carotene than the American and Mexican grown varieties.

FREDEEN, Kansas City, Mo.

VITAMIN E LEVELS IN MATERNAL AND FETAL BLOOD PLASMA. JON V. STRAUMFJORD and MARY LOUISE QUAIFE, Proc. Soc. Exp. Biol. & Med. **61**:369 (April) 1946.

Plasma vitamin E values were found to be higher in the latter half of pregnancy than early and higher than in nonpregnant women and in male subjects. Study of cord blood and venous blood of 54 mothers disclosed values of 1.70 plus or minus 0.30 mg. per hundred cubic centimeters for the mothers to 0.34 plus or minus 0.12 mg. for the cord blood. The vitamin E level thus appears to increase in pregnancy just as it has been found with plasma lipids. Similarly both the vitamin E level and the plasma lipids are low in fetal plasmas. No sex difference was found in the vitamin E levels of newborn infants.

HANSEN, Galveston, Texas.

Acute Contagious Diseases

EFFECT OF CATIONIC DETERGENTS IN COTTON RATS: NEUTRALIZING EFFECT OF CETAMIUM AGAINST POLIOMYELITIS VIRUS. J. A. TOOMEY and W. S. TAKACS, Arch. Pediat. **62**:337 (Aug.) 1945.

A series of experiments is reported in which various dilutions of "zephiran chloride" N. N. R. (benzalkonium chloride), "phemerol chloride" N. N. R. ([p-(2-methyl-4,4-dimethyl pentano-2) (phenoxy-ethoxy-ethyl)] dimethyl benzyl ammonium chloride monohydrate), "ceepryn" (cetyl pyridium chloride) and "cetamium" (cetyl trimethyl ammonium bromide) were tested on white rats. The animals were found to tolerate 0.125 per cent solutions of each. In a second group of studies 0.125 per cent solution of "cetamium" failed to neutralize either the Flexner strain or the Trask SK strain of poliomyelitis virus.

GRULEE JR., Evanston, Ill.

RUBELLA IN PREGNANCY CAUSING MALFORMATIONS IN NEWBORN. MAX J. FOX and MORTIMER M. BORTIN, J. A. M. A. **130**:568 (March 2) 1946.

Of 22,226 cases of rubella reported to the Milwaukee City Health Department in 1942, 1943 and 1944, 11 occurred in pregnant women. In 5 cases the disease occurred in the first two months, in 4 cases in the second to fourth month, in 1 case in the seventh month and in 1 case in the ninth month. One stillbirth of a hydrocephalic child occurred among the 11 cases and 1 other child had a hydrocephalus which receded so that the child is now normal. All the other pregnancies resulted in normal children, one woman having normal twins. One mother had previously had a child with bilateral congenital cataracts, but the pregnancy complicated by rubella resulted in a normal child.

"Our records do not justify consideration of termination of pregnancy because of rubella."

BAIRD, Wauwatosa, Wis.

TREATMENT OF SCARLET FEVER. PAUL ASHLEY, J. A. M. A. **130**:771 (March 23) 1946.

The report covers 298 patients with scarlet fever treated in June and July 1945. A high percentage of the cases were due to sulfonamide-resistant streptococci.

Results of use of antistreptococcus serum and of convalescent serum were roughly proportional to the toxicity of the patient. Reactions were commoner after use of antistreptococcus serum. Best results with convalescent serum were obtained if the incidence of a type of streptococcus in the source group was similar to that in the treated group.

The treatment of choice for scarlet fever is convalescent serum given in doses proportional to the toxicity of the patient and penicillin given until the temperature has been normal for five days.

BAIRD, Wauwatosa, Wis.

CURARE IN THE TREATMENT OF ACUTE POLIOMYELITIS. MAX J. FOX, J. A. M. A. **131**:278 (May 25) 1946.

Curare was given to 34 patients in the acute stage of poliomyelitis. The ages ranged from 3 to 33 years. Dosage was roughly 0.9 mg. of curare per kilogram of body weight. Twelve patients noted subjective improvement, but this was transient. Twenty patients showed minor objective improvement but in only 2 was relaxation of spasm certain. Five patients with bulbar poliomyelitis did not respond to the drug, 1 having a progressively downhill course necessitating the use of a respirator.

"Curare may be in some instances of temporary benefit, but it is a dangerous drug and is not to be encouraged for the treatment of the acute phase of poliomyelitis."

BAIRD, Wauwatosa, Wis.

MUMPS INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM. EUGENE M. HOLDEN, ARCHIE Y. EAGLES and JOHN E. STEVENS JR., J. A. M. A. **131**:383 (June 1) 1946.

One hundred consecutive cases of mumps seen at an army hospital were studied to determine the incidence of involvement of the central nervous system.

Thirty-three patients had clinical signs of meningoencephalitis, stiff neck, headache and/or drowsiness; 5 of these patients had no abnormalities in their spinal fluid.

Two patients without clinical symptoms showed an increased number of cells in the spinal fluid and increased protein. Six additional patients without symptoms had increased protein and 2 additional ones an increased cell count.

There was no correlation between the severity of the parotid involvement or the presence of epididymo-orchitis and the occurrence of involvement of the central nervous system.

BAIRD, Wauwatosa, Wis.

AN OUTBREAK OF POLIOENCEPHALITIS AMONG NAVY CADETS, POSSIBLY FOOD BORNE. DAVID M. GOLDSTEIN, W. McD. HAMMON and HENRY R. VIETS, J. A. M. A. **131**:569 (June 15) 1946.

An explosive outbreak of poliomyelitis occurred at a West Coast naval training school during the first week of September 1945. There were 18 clinical cases and over 100 cases with suggestive symptoms all having onset during an eight day period. No secondary cases occurred. Encephalitic manifestations predominated, but poliomyelitis virus was isolated from the stools of 3 of the 4 patients tested. After a careful epidemiologic investigation the evidence pointed to contaminated milk as the source of the infection. The milk had a high bacterial count and was exposed to flies which had access to human and animal feces.

BAIRD, Wauwatosa, Wis.

PROPHYLAXIS OF DIPHTHERITIC PARALYSIS WITH SHOCK DOSES OF VITAMIN B-1. A. COLARIZI and S. SANTYAN Y VELASCO, Riv. di clin. pediat. **44**:129 (March) 1946.

With a view to surveying whether vitamin B_1, given in shock doses at the beginning and during diphtheria is capable of preventing and influencing the process of diphtheritic paralysis, the authors have followed for about twenty-seven months 100 diphtheritic children treated with specific serum only, and 100 treated both with serum and with high doses of thiamine hydrochloride hypodermically (50 with 100 mg. at the beginning of diphtheria and 50 with a total dose of 200 mg., having been given the 100 mg. dose again on the ninth or tenth day).

The results have shown that the shock doses of vitamin B_1 reduced the number of cases of paralysis and considerably limited their spreading and seriousness.

We can accept that hypovitaminosis B_1 shares in the mechanism of diphtheritic paralysis and that thiamine previously introduced prevents or limits the trophic damage to the nervous tissue.

AUTHORS' SUMMARY.

OCCURRENCE, DIAGNOSIS AND PROGNOSIS OF TOTAL AURICULOVENTRICULAR BLOCK IN DIPHTHERIA. P. SCHWEITZER, Nederl. tijdschr. v. geneesk. **90**:44 (Jan. 19) 1946.

The recognition of those diphtheritic diseases of the heart in which toxic degenerative changes in the heart muscle give rise to a total dissociation between auricle and ventricle is not always simple. On the other hand, the prognosis of this severe change is not so bad as is generally accepted. The author investigated, in the course of two years, 30 patients showing this change both clinically and on the electrocardiogram. They all were suffering from toxic diphtheria. The albuminuria was often more than 10 per cent (Esbach), and this is regarded as an unfavorable sign. In these cases often a hemorrhagic diathesis was present. The age of these patients with a total auriculoventricular block ranged between 2 and 25 years. The danger of the occurrence of the total block arises about a week after the onset of the disease; the myocarditis itself starts in these cases after a few days. In 1 patient the block appeared on the fifteenth day.

The recognition of the total block in patients with diphtheria is difficult because it is usually combined with a rapid action of the heart. One patient even had a total block combined with a ventricular rate of 140. Attacks of the Adams-Stokes syndrome were observed only in some patients with an extremely slow ventricular rate. The most definite symptom that makes probable the occurrence of a total auriculoventricular block in diphtheria is the sudden decrease in the pulse rate. Less characteristic symptoms which make a total block probable are: an acute decompensation with congestion of the liver, vomiting and general unrest occurring in the beginning of the diphtheria and a sudden irregularity of the pulse. Once the occurrence of the block was combined with anginal pains. The diagnosis of a total auriculoventricular block is made by electrocardiographic investigation.

The duration of the block varied from some minutes to nine days. Only those patients who had an extremely slow ventricular rate with attacks of the Adams-Stokes syndrome were treated (150 to 200 mg. of synthetic racemic ephedrine hydrochloride daily, a treatment which slightly improved the rhythm).

Of the 30 patients 23 died and 7 recovered. Patients with myocarditis were mobilized only when the T waves were positive in at least two leads and had become flat in the third lead.

VAN CREVELD, Amsterdam, Netherlands.

TWO AND A HALF YEARS OF DIPHTHERIA IN A TOWN PRACTICE. K. MARANG and C. J. BARENTS, Nederl. tijdschr. v. geneesk. **90**:83 (Feb. 2) 1946.

The authors survey the cases of diphtheria in the town of Utrecht (Holland) from September 1942 until February 1945. The total number of cases was 6,367, of which 391 were fatal. The mortality below the age of 13 years was much higher than above this age. In 5 patients relapses of diphtheric membranes on the tonsils occurred respectively on the twelfth, fifteenth, seventeenth, nineteenth and twenty-ninth day of the disease.

VAN CREVELD, Amsterdam, Netherlands.

DIPHTHERIA. F. J. A. HUYGEN, Nederl. tijdschr. v. geneesk. **90**:127 (Feb. 16) 1946.

The author describes 5 cases of a relapse of diphtheria within one year after a true, classic diphtheritic angina.

VAN CREVELD, Amsterdam, Netherlands.

EPIDEMIC OF POLIOMYELITIS IN WESTERBORK CONCENTRATION CAMP (HOLLAND) IN AUGUST AND DECEMBER 1943. N. SPEYER, Nederl. tijdschr. v. geneesk. **90**:130 (Feb. 16) 1946.

This epidemic of poliomyelitis in a concentration camp for adults and children included 58 cases, of which 21 cases were in children below the age of 5 years and 30 cases in patients above the age of 15 years. The youngest patient was 6 weeks old. The population of the camp was about nine thousand persons. In this epidemic the incubation period ranged between one and three weeks.

Forty-one per cent of the cases were abortive, and in 59 per cent paralysis resulted.

The effect of injections of reconvalescent serum remained uncertain. In a fairly large number of cases the patients complained of intense fatigue, which sometimes lasted some months. Of the 58 cases 25 were of the spinal form, 9 of the bulbopontile form, 21 of the meningeal form and 3 of the encephalitic form of the disease. The quick isolation of the patients with abortive disease probably explains why this epidemic remained restricted.

VAN CREVELD, Amsterdam, Netherlands.

ADMINISTRATION OF DESOXYCORTICOSTERONE ACETATE IN DIPHTHERIA. H. A. HANSEN-YMKER, Nederl. tijdschr. v. geneesk. **90**:208 (March 16) 1946.

No therapeutic results were seen from the injection of desoxycorticosterone acetate in a number of cases of malignant diphtheria.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

CLINICAL TETANUS: A STUDY OF FIFTY-SIX CASES WITH SPECIAL REFERENCE TO THE METHODS OF PREVENTION AND A PLAN FOR EVALUATING TREATMENT. EDWARD L. PRATT, J. A. M. A. **129**:1243 (Dec. 29) 1945.

This is the report of 56 cases of tetanus treated in the Infants' and Children's Hospitals at Boston from 1924 to 1944. There were 24 deaths.

Administration of amounts of antitoxin up to 80,000 units was not more effective than of 30,000 units.

Although intrathecal administration was suggestively more effective the occurrence of fatal reaction following this method indicates it should be used, if at all, only in the cases of most severe disease.

Excision of the site of infection did not ameliorate the course of the disease once clinical symptoms had appeared.

A high percentage (80) of cases followed infections or accidents which would not ordinarily require antitoxin or even (in 60 per cent of cases) a tetanus toxoid booster dose. Hence the production and maintenance of active immunity is the only way of reducing the incidence of the disease.

BAIRD, Wauwatosa, Wis.

PHYSICAL RECONDITIONING AFTER RHEUMATIC FEVER. PETER V. KARPOVICH, MERRITT P. STARR, ROBERT W. KIMBRO, CHARLES G. STOLL and RAYMOND A. WEISS, J. A. M. A. **130**:1198 (April 27) 1946.

The time of beginning and intensification of training among 88 patients convalescing from rheumatic fever at an Army Air Forces hospital was controlled by a series of physical fitness tests. These tests were found to be a simple and safe method of control over reconditioning. Patients could safely participate in the system of graded physical exercises within two weeks after the rheumatic fever became quiescent as determined by normal temperature, normal electrocardiogram, sedimentation rate of 15 mm. or less (Westergren method) and absence of

arthralgia. The delay in beginning physical reconditioning was reduced from 77.3 days to 16.2 days without an increase in the incidence of cardiac damage during a six to twelve month observation period. There was no relationship between the sedimentation rate area (height of abnormal sedimentation rate plotted against days of hospitalization) and the time necessary to obtain a "fair" rating on the tests.

BAIRD, Wauwatosa, Wis.

THE PROTECTIVE EFFECT OF VACCINATION AGAINST EPIDEMIC INFLUENZA B. THOMAS FRANCIS JR., JONAS E. SALK and WILLIAM M. BRACE, J. A. M. A. **131**:275 (May 25) 1946.

During an epidemic of influenza B in November and December 1945 at the University of Michigan it was possible to compare the incidence of the disease in an army unit of 600 men which had been vaccinated against influenza and another service unit of 1,100 men which had not. The incidence among the vaccinated was 1.15 per cent; in the unvaccinated, 9.91 per cent.

The strains of virus encountered differed serologically from the Lee strain of type B influenza virus included in the vaccine, but this did not appear to prevent the prophylactic effect of the vaccine.

The epidemiologic pattern exhibited by influenza B was a continuous prevalence for a period of at least twelve months, representing an endemic disease with numerous epidemic upsurges.

The evidence clearly indicates that the subcutaneous vaccination with inactivated influenza virus types A and B exerted a striking protective effect against epidemic influenza B.

AUTHORS' SUMMARY.

HEMOGLOBIN METABOLISM AND INTERNAL LEISHMANIASIS. ANTONIO CROSCA, Riv. di clin. pediat. **44**:141 (March) 1946.

The author has studied the alterations in the hemoglobin metabolism in 21 children from 1 to 7 years old, affected by internal leishmaniasis, noting an almost constant increase in the metabolism of hemoglobin. The bilirubin in the blood is increased in many cases, and the fragility test often shows an increase in the maximum resistance of the red blood cells, while the minimum resistance is decreased. There are signs of hematic regeneration with a frequent increase in the reticulocytes.

The author believes that the hemolysis may be related to an increased hemocatheretic function of the reticuloendothelial system, which, as is now recognized by every one, is hypertrophic and hyperplastic in internal leishmaniasis, and that in the pathogenesis of anemia in internal leishmaniasis hyperhemolysis plays an important part.

AUTHOR'S SUMMARY.

CONTRIBUTION TO KNOWLEDGE OF HEMATOLOGIC ALTERATIONS IN ANCYLOSTOMIASIS IN CHILDHOOD. T. AVERSA, Riv. di clin. pediat. **44**:193 (April) 1946.

The author, after having reviewed the hematologic alterations found in ancylostomiasis, which have been systematically studied only in adults, and the various theories explaining the anemia present in this disease, reports his results for 4 children with ancylostomiasis. He concludes that in his cases the anemia is hypochromic, with slight signs of peripheral regeneration, but in any case more evident than in adults: leukocytes are normal or slightly increased. The white blood cell differential count revealed eosinophilia and fewer monocytes, a normal or slightly increased number of platelets and no signs of hyperhemolysis. In the fragility test for red blood cells the resistance is increased; in the bone marrow erythroblastic hyperplasia is present, in an even greater degree than in adults, with a stoppage in

maturation and inhibition of the karyokinetic process. The clotting time and the retraction of the coagulum are accelerated. According to the author these findings correspond to the most recent pathogenic interpretations, which place anemia from ancylostomiasis in relation to toxic-inhibitory and deficiency factors.

AUTHOR'S SUMMARY.

PARATYPHOID TRANSMITTED BY SMOKED EEL. G. D. SEMMES, Nederl. tijdschr. v. geneesk. **90**:80 (Feb. 2) 1946.

The author describes paratyphoid B (Salmonella schottmüller) in a village and in a small town, transmitted by smoked eel. Insufficient smoking of the infected eel probably had caused the epidemic.

VAN CREVELD, Amsterdam, Netherlands.

INFECTION WITH BALANTIDIUM COLI. S. L. BRUG and H. VERHAGEN, Nederl. tijdschr. v. geneesk. **90**:93 (Feb. 2) 1946.

The author reports on a case of Balantidium coli in a boy 1½ years old. No contact with pigs could be ascertained. No symptoms accompanied the infection. The action of different medicaments on Balantidium organisms was studied in vitro but none of them killed the organisms in five minutes.

VAN CREVELD, Amsterdam, Netherlands.

OXYURIASIS: DO THE LARVAE OF OXYURIS VERMICULARIS PENETRATE FROM NORMAL HUMAN INTESTINE INTO THE INTERNAL STRUCTURES IN MEN? F. H. SMALT, Nederl. tijdschr. v. geneesk. **90**:333 (April 20) 1946.

If it is true that the larvae of Oxyuris vermicularis penetrate from normal human intestines into the internal structures, the author expected to find at autopsy in cases of severe infection with Oxyuris different stages of the parasite from the egg to the sexually ripe worm, and especially those forms which could be expected to be present in the interior structure and not in the lumen of the intestine. This means that for Oxyuris the larva of which, just issued from the egg, has the dimensions 10 by 150 microns, one had to look especially for larvae about 150 microns to 1.2 mm. in size.

At the eighth autopsy, that of a child of 2 years, who died of general tuberculosis, an extensive Oxyuris infection was found. In this case one larva of Oxyuris vermicularis was found in the centrifugate of the scrapings and feces of the jejunum. This larva, as regards total length and other characteristics, should have been absent from the intestine if habitual penetration into the intestinal lumen occurred. The total length of this larva was 277 microns. The author is of the opinion that he has demonstrated in this case in the jejunum just the link which should fail if in Oxyuriasis, as in ascariasis, perforation into the interior structures should occur.

VAN CREVELD, Amsterdam, Netherlands.

SMOKED EEL AS CARRIER OF PARATYPHOID. C. J. H. VAN DEN BROEK, Nederl. tijdschr. v. geneesk. **90**:416 (May 4) 1946.

By injection of a small amount of a twenty-four hour suspension of Escherichia coli into a number of eels, followed by smoking of the eels during different periods of time, and after the smoking, counting the number of organisms in a piece of muscle tissue in which the organisms were injected, it could be established that only a thorough smoking guarantees the killing of all pathogenic micro-organisms eventually present in the eels. A perfect smoking can be determined from the color and from the "well done" state of the muscular tissue of the eel.

VAN CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

PENICILLIN TREATMENT OF THE SYPHILITIC INFANT. NORMAN R. INGRAHAM JR., JOHN H. STOKES, HERMAN BEERMAN, JOHN W. LENTZ, PAUL GYORGY and ELIZABETH K. ROSE, J. A. M. A. **130**:694 (March 16) 1946.

Continued experience with sodium penicillin given by intramuscular injection indicates that it is a satisfactory treatment for infantile congenital syphilis.

Twenty-six infants have been treated. Twenty-one are alive, and of these, 11 have serologically negative reactions and the reactions of 3 are becoming less seropositive. The 5 deaths have not been due to penicillin. Forty per cent show a reaction to therapy consisting of fever and gastrointestinal symptoms. Careful judgment is necessary in the treatment, and debilitated infants need expert pediatric care.

Of the babies followed more than six months 10 (71 per cent) are clinically normal and give a seronegative reaction, and 4 are clinically normal but give a seropositive reaction.

An increase of dosage over the 20,000 Oxford units per pound (44,092 per kilogram) total is suggested, total dosages up to 74,000 per pound (163,139 per kilogram) having been given. Increasing the period of treatment from seven or eight to ten or fifteen days is also recommended.

BAIRD, Wauwatosa, Wis.

THE CHANGING CHARACTER OF COMMERCIAL PENICILLIN WITH SUGGESTIONS AS TO THE USE OF PENICILLIN IN SYPHILIS. COMMITTEE ON MEDICAL RESEARCH, THE UNITED STATES HEALTH SERVICE AND THE FOOD AND DRUG ADMINISTRATION, J. A. M. A. **131**:271 (May 25) 1946.

Commercial penicillin is a mixture in which at least four species have been identified. These are known in the United States as penicillins G, X, F and K. Penicillin K is less effective therapeutically apparently because it is rapidly destroyed in the body. The content of the various types in commercial penicillin varies. Some recent commercial preparations have contained more of K. The increasing "purity" of commercial penicillin may also have affected its potency. Further study of the factors affecting the potency of commercial penicillin are being made.

BAIRD, Wauwatosa, Wis.

Diseases of the Blood, Heart and Blood Vessels and Spleen

PURE CONGENITAL PULMONARY STENOSIS. A. N. FREED and J. BUDNITZ, Am. Heart J. **31**:369 (March) 1946.

The authors report the case of an infant with pure pulmonary stenosis who died at the age of 11 months. The baby had been irritable since birth and had rapid and noisy respiration, and the heart rate was rapid. Physical examination revealed pronounced cardiac enlargement with a systolic thrill, and a loud harsh high-pitched systolic murmur, maximum over the pulmonary area. At the age of 10 months the baby began to fail. Symptoms and signs of congestive heart failure were present for five weeks before death. Autopsy revealed complete fusion of the leaflets of the pulmonary valve with an opening only 2 mm. in diameter. The right auricle and right ventricle were significantly dilated and hypertrophied.

The authors emphasize the rarity of congenital pulmonary stenosis unassociated with other cardiac defects.

GIBSON, Chicago.

TRAUMATIC RUPTURE OF THE SPLEEN IN CHILDHOOD. H. WILLIAM SCOTT JR. and J. ROBERT BOWMAN, J. A. M. A. **130**:270 (Feb. 2) 1946.

This is a report of the 7 cases of traumatic rupture of the spleen seen by the surgical service of the Children's Hospital of Boston during the period 1937 to 1944 inclusive. All the children were boys. The ages ranged from 4 to 13 years. Three

boys were injured in falls, 3 in sledding accidents and 1 by a blow. There were no associated rib fractures, and only 1 case showed any superficial evidence of trauma. All recovered after splenectomy.

"A history of trauma to the abdomen, followed by symptoms and signs of loss of blood with abdominal tenderness and spasm maximal in the left upper quadrant and a reduced or falling red blood count, are diagnostic of intra-abdominal hemorrhage and strongly suggestive of rupture of the spleen." Roentgenograms are indicated in order to exclude associated injuries. After the presumptive diagnosis is made surgical treatment is indicated with splenectomy if even a seemingly trivial splenic laceration is found. Plasma and adequate amounts of whole blood must be given before, during and after operation. Postoperative thrombosis due to a high platelet count may occur and should be treated by heparinization.

BAIRD, Wauwatosa, Wis.

FOLIC ACID THERAPY IN THE ANEMIAS OF INFANCY AND CHILDHOOD. WOLF W. ZUELZER, J. A. M. A. **131**:7 (May 4) 1946.

A megaloblastic anemia occurring in white children under 18 months of age is characterized by (1) the presence of a severe normochromic anemia, usually macrocytic, (2) a tendency toward leukopenia and neutropenia with associated presence of giant metamyelocytes and "macropolycytes," (3) a decrease in platelets and (4) an atypical bone marrow pattern resembling that of pernicious anemia in relapse.

Twelve of 29 patients with this syndrome were treated with folic acid. Three patients died of severe infections before the results could be evaluated. The other 9 showed a good response, with rise in reticulocyte count, in hemoglobin and in red cell count and with a return of the marrow to normal. Follow-up studies for periods up to ten months have shown no relapses.

In no other type of anemia in children was folic acid found to be of value.

BAIRD, Wauwatosa, Wis.

A CASE OF PERIARTERITIS NODOSA WITH DECEREBRATE RIGIDITY AND EXTENSIVE ENCEPHALOMALACIA IN A FIVE YEAR OLD CHILD. N. MALAMUD, J. Neuropath. & Exper. Neurol. **4**:88 (Jan.) 1945.

Malamud reports the case of a 5 year old boy who, while convalescing from an infection of the upper respiratory tract, had fleeting pains in the joints and abdomen. Examination revealed a systolic cardiac murmur, elevated temperature and leukocytosis but no swelling or redness of the joints. Acute rheumatic fever was suspected. One week later the symptoms began to subside, but the patient suddenly had a series of seizures, became comatose and exhibited decerebrate rigidity. Tendon reflexes could not be elicited, and there were no signs of involvement of the pyramidal tract. The pupils were dilated and fixed to light, and there was mild papilledema. Lumbar puncture and studies of the cerebrospinal fluid revealed nothing significant. Ventriculographic studies suggested the presence of a tumor of the brain stem. The patient died about two and a half months after the onset of his illness.

There was massive necrosis of the cerebrum, while the brain stem and cerebellum were of normal consistency and the basal vessels were soft and delicate. Microscopic observation revealed complete destruction of the cytoarchitecture, with few or no nerve cells remaining, and the brain tissue was replaced with vacuoles of varying sizes or with amorphous masses of precipitate. Within the necrotic tissue a very active mixed mesenchymal and glial reaction occurred. There were marked proliferation of microglia and an equally intense proliferation of reticulin fibers, with newly formed blood vessels. The neuroglial reaction was moderate. In the leptomeninges there were a few polyblasts and lymphocytes. The white matter showed intense, but more patchy, involvement. Extensive necrotic changes were also observed throughout the optic chiasm, the caudate

nucleus, the putamen and the globus pallidus. The thalamus, with the exception of the centromedian and intralaminar nuclei, was destroyed, partly as the result of secondary degeneration. The hypothalamus and the subthalamus were only slightly involved. The necrosis terminated at the level of the red nucleus. The brain stem and the spinal cord exhibited only mild secondary degeneration of the pyramidal tracts. The cerebellum, however, showed pronounced diffuse degeneration of nerve cells in the Purkinje layer and the dentate nucleus. Study of the meningeal and cerebral blood vessels revealed lesions in a subacute phase of hyaline necrosis of the subintima and media, perivascular infiltration with lymphocytes and fibroblastic proliferation of adventitia and intima, encroaching on the lumen. Similar vascular lesions were observed in the heart, and somewhat more chronic ones were noted in the walls of the trachea, the esophagus and the gastrointestinal tract and in the kidneys.

Anatomically, there was a conspicuous discrepancy between the extensive destruction of the cerebral parenchyma and the restricted vascular lesions. The discrepancy between the involvement of the parenchyma and that of the vascular system may be of significance in understanding the nature of the disease. Malamud states that the onset following an infection of the upper respiratory tract and its initial general effect on various organs, followed by an intense necrotizing process in the brain, clearly out of proportion to the extent of the arteritis, suggest an allergic reaction.

GUTTMAN, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

HEREDITY OF RH BLOOD TYPES: V. IMPROVED NOMENCLATURE; ADDITIONAL FAMILY STUDIES WITH SPECIAL REFERENCE TO HR. ALEXANDER S. WIENER, EVE B. SONN and H. R. POLIVKA, Proc. Soc. Exper. Biol. & Med. **61**:382 (April) 1946.

Hereditary transmission of the eight Rh blood types in 300 families with 620 children was investigated and the results were in conformity with the theory of six major allelic genes. Studies of the Hr factor in 81 families with 126 children and on a random series of 645 Caucasians in New York city support the theory that factors Rh and Hr are related genetically and serologically like agglutinogens M and N. The authors state that the Hr factor considerably increases the chances of exclusion in cases of disputed parentage and cite an instance of a court decision primarily on the basis of the results of blood tests. HANSEN, Galveston, Texas.

PATHOGENESIS OF ERYTHROBLASTOSIS FETALIS. ALEXANDER S. WIENER, Proc. Soc. Exper. Biol. & Med. **61**:390 (April) 1946.

The author's present theory of erythroblastosis fetalis regarding clinical manifestations and type of isoantibody present in the maternal serum is discussed.

Congenital Hemolytic Disease.—This syndrome is caused by the presence in the maternal serum of univalent antibodies specific for fetal red cells. With small amounts of antibody in the fetal circulation the infant contracts an anemia which responds to proper transfusions. With larger amounts there is sufficient anemia to cause anoxemia of capillary walls with exudation of serum proteins into tissue spaces and invariably fetal hydrops. Pronounced pallor, ascites, anasarca, splenomegaly and hepatomegaly are present, and microscopically there are islands of extramedullary hemopoiesis of the liver and spleen with deposits of hemosiderin.

Erythroblastosis Proper.—During labor and delivery agglutinins which are presumably larger molecules than blocking antibodies find their way into the fetal circulation. Jaundice develops in a few hours in the infant, who appears healthy at birth, feeds poorly, becomes stuporous, maybe with convulsions, coma and death. Agglutination thrombi in the smaller vessels result in damage to the liver and the brain. The kernicterus is not caused by jaundice itself, but represents a staining reaction of damaged ganglion cells. Few of these infants survive.

HANSEN, Galveston, Texas.

PERNICIOUS ANEMIA IN CHILDHOOD. R. GIUNTINI, Rev. di clin. pediat. **44**:207 (April) 1946.

From a complete review of all the scientific contributions to pernicious anemia in children, to which 2 cases observed personally by the author are added, it appears that only 7 certain cases of pernicious anemia in childhood have been reported up to now. To these a few other cases can be added in which this diagnosis can be accepted with some reservations. On the basis of these statistical data the author describes the clinical and blood-bone marrow picture found in this disease in children. The resemblance and the particular characteristics which differentiate pernicious anemia in children and adults are described in detail.

AUTHOR'S SUMMARY.

NEW METHOD OF MEASURING THE AMOUNT OF "ALKALINE" PHOSPHATASE IN BLOOD SERUM. G. VAN VEEN, and A. M. DE ROOCK, Nederl. tijdschr. v. geneesk. **90**:21 (Jan. 5) 1946.

The authors describe a micromethod for the determination of "alkaline" phosphatase in which the formed amount of inorganic phosphate is transferred into an insoluble barium salt. This product remains in colloidal solution, and the quantity of barium phosphate is measured with the photometer. Preceding precipitation of the proteins of the serum thus is not necessary.

VAN CREVELD, Amsterdam, Netherlands.

DEPOSIT OF CALCIUM IN THE HEART IN YOUTH. F. S. P. VAN BUCHEM, Nederl. tijdschr. v. geneesk. **90**:459 (May 11) 1946.

A girl 18 years old had had collapses intermittently for fifteen years. In walking she often became tired soon and complained of anginal pains. Dyspnea increased in her last years. Several calcium shadows were visible in the roentgenograms of the heart. The clinical picture seemed to point to a primary pulmonary sclerosis. Death occurred under the symptoms of decompensation of the heart.

At autopsy chronic partial endocarditis of the left ventricle and auricle with calcification was found. The author discusses the possible pathogenesis.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Nose, Throat and Ear

BACTERIOLOGIC OBSERVATIONS DURING EPIDEMIC OF OTITIS MEDIA AND OF MASTOIDITIS. A. VEDDER, Nederl. tijdschr. v. geneesk. **90**:291 (April 13) 1946.

In 1944 the author was able to observe an epidemic of otitis media and of mastoiditis in one of the concentration camps in Holland. This epidemic affected children especially and was not preceded by another disease. The complications (like mastoiditis) arose early and quickly in this epidemic and at operation great destruction was found, while the wound healed badly. The bacteriologic investigation showed that at first at paracentesis only pneumococci could be isolated, but that these soon were supplanted by hemolytic streptococci, both in the middle ear and in the mastoid.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Lungs, Pleura and Mediastinum

PULMONARY CALCIFICATION AND SENSITIVITY TO HISTOPLASMIN, TUBERCULIN AND HAPLOSPORANGIN. AMOS CHRISTIE and J. C. PETERSON, J. A. M. A. **131**:658 (June 22) 1946.

Three hundred and forty-four children between the ages of 5 and 19 years, all living in Tennessee, were tested for their sensitivity to tuberculin (0.1 mg.), histoplasmin and haplosporangin (an antigen derived from a fungus known to give

granulomatous pulmonary lesions in some rodents). Seventy-four children reacted to tuberculin, 252 to histoplasmin and none to haplosporangin. One hundred and eighty-three of the children had intrathoracic calcifications visible on roentgenographic examination.

Of the children showing calcifications 42 had positive reactions to both histoplasmin and tuberculin, 7 to tuberculin only, 120 to histoplasmin only and 14 to neither. Of these last only 2 had pronounced calcification. Of the 161 children without calcifications 18 had positive reactions to both, 7 to tuberculin only, 72 to histoplasmin only and 64 to neither.

This study suggests a relationship between sensitivity to histoplasmin and the presence of pulmonary calcifications.

BAIRD, Wauwatosa, Wis.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

PAROXSMAL ABDOMINAL PAIN: A FORM OF FOCAL SYMPTOMATIC EPILEPSY. MATTHEW T. MOORE, J. A. M. A. **129**:1233 (Dec. 29) 1945.

"Clinical study of 6 patients (2 children, 4 adults) in whom paroxysmal abdominal pain was either the only symptom or the dominant one revealed this to be a type of epileptic variant (abdominal epilepsy). . . . Criteria for diagnosis are based on (1) exclusion of intrinsic visceral disease, (2) adequate historical data, (3) attack pattern of an epileptic order, (4) associated epileptic show, (5) objective evidence of cerebral organic disease or dysfunction and (6) effect of anticonvulsant drugs on the symptom of abdominal pain and on the electroencephalogram."

BAIRD, Wauwatosa, Wis.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS. WILLIAM E. LADD, PAUL F. WARE and LAWRENCE K. PICKETT, J. A. M. A. **131**:647 (June 22) 1946.

This is the report of an additional 380 patients operated on by various members of the surgical service at the Children's Hospital of Boston since 1939, making a total of 1,145 operated on since 1915.

The pathologic change is hypertrophy of the circular layer of the pylorus. Clinical findings include dehydration, projectile vomiting, scanty stools and urine, visible gastric waves and a palpable tumor. A new symptom complex to be differentiated is "chalasia of the esophagus," in which, on roentgenologic examination, the gastric cardia is continuously relaxed and barium given is frequently regurgitated.

Preoperative fluid therapy is important. Treatment is pyloromyotomy with the patient under ether anesthesia, preferably through a Robertson gridiron incision. Complications include duodenal perforation (less serious if recognized and closed at operation), otitis media, pneumonia, wound infection, evisceration and severe diarrhea.

There were 4 deaths in the 380 cases. One baby had pneumonia, 1 diarrhea and 2 others congenital defects. Recently there have been operations in 225 consecutive cases without a fatality.

BAIRD, Wauwatosa, Wis.

DYSPORIA ENTEROBRONCHOPANCREATICA CONGENITA FAMILIARIS: CYSTIC FIBROSIS OF THE PANCREAS. E. GLANZMANN, Ann. pædiat. **166**:289 (June) 1946.

A report is made of a new case of meconium ileus in which the patient survived the first week but later contracted a severe "pertussoid" and emphysema with other pulmonary complications. In a second case of "pertussoid" a right-sided obstructive emphysema is described for the first time which was caused by valvular occlusion of a bronchus with tenacious secretion. The same case presented further familial hypoproteinemia and hypoglobulinemia, hitherto not observed with this illness. A third case showed the familiar picture of celiac syndrome with chronic

pneumonia and formation of abscess in the upper lobe of the right lung. The different clinical pictures, including also cystic fibrosis of the pancreas, are united under the heading "dysporia enterobronchopancreatica congenita familiaris." "Dysporia" means here—primarily as a clinical description—"a difficult way," "a hindrance of passage of secretions," caused either by the abnormal physicochemical qualities of these secretions or, less often, by congenital stenosis of these systems of canals. The fibrosis of the pancreas is not considered to be the determining factor of meconium ileus and of the changes in the bronchial system; it might, on the other hand, perhaps be made responsible for the secondary celiac syndrome. For the first time erythroblastosis fetalis is found in conjunction with meconium ileus. A relationship, further supported by analogous occurrence in siblings, with the illnesses belonging to the erythroblastosis complex, is thus emphasized. In the present 3 cases it could further be demonstrated that the mother was Rh negative and the child Rh positive. It is assumed that Rh-like antibodies penetrate via the liquor amnii into the canal systems of intestine, lungs and pancreas, react there against antigens produced by the respective organ cells, and thereby produce persistent damage to the glandular cells which manifests itself by creating an abnormally tenacious secretion with all its consequences for dysporia.

AUTHOR'S SUMMARY.

DYSPORIA ENTEROBRONCHOPANCREATICA CONGENITA FAMILIARIS: CYSTIC FIBROSIS OF THE PANCREAS. PAUL RINIKER, Ann. pædiat. **166**:314 (June) 1946.

Glanzmann's dysporia enterobronchopancreatica congenita familiaris is anatomically characterized by occlusions and stenoses, caused by inspissated mucous and serous secretions in the bronchi and pancreas and not infrequently in the intestine.

The mucous bronchial stenoses lead to atelectasis and emphysema, followed by bronchopneumonic abscesses and pleurisy. These sequelae are the most frequent cause of death in dysporia.

Under the influence of inspissated secretions there takes place, in the latter part of the fetal period, intralobular cystic transformation in the pancreas with secondary fibrosis, causing obliteration in the acini and sometimes also in the ducts.

Occlusions and secondary ectases also occur in the larger bile ducts, while formation of accessory biliary ducts happens in the Glisson capsules of the liver. Sometimes meconium ileus is produced in the small intestine of the fetus by stagnation of thickened mucous masses.

The pathogenesis of the various anatomic changes points uniformly to a disturbance in the enterobronchial canal systems caused by an abnormal viscosity of the secretions.

Cornelia de Lange recognized that familial dysporia is caused by damage to the fetus from maternal toxins.

AUTHOR'S SUMMARY.

SERUM PHOSPHATASE IN PATIENTS WITH JAUNDICE. P. VAN DER MEER, Nederl. tijdschr. v. geneesk. **90**:171 (March 2) 1946.

The "alkaline" phosphatase was determined, according to the method of King and Armstrong, in 52 patients suffering from different forms of jaundice. The author concludes that a normal or slightly increased phosphatase content (not exceeding 20 units), combined with a distinctly increased bilirubin content of the serum, excludes a mechanical cause of the jaundice.

VAN CREVELD, Amsterdam, Netherlands.

PLAUT-VINCENT DISEASE. A. P. VAN DER WEY, Nederl. tijdschr. v. geneesk. **90**: 211 (March 16) 1946.

The author describes three forms in which Plaut-Vincent disease can manifest itself in the mouth: as gingivitis, as the typical angina and as multiple flat ulcers.

Though the danger does not lie in the serious character of the disease, it may give rise to a severe morbid picture, caused by transfer of infectious material to the lungs, which can take place especially during narcosis. In these cases often a pulmonary abscess may develop. When regular rinsing of the mouth with hydrogen dioxide does not result in significant improvement within a few days, local treatment with a 10 per cent solution of neoarsphenamine in glycerin is indicated or, if this does not help, one or two intravenous injections of neoarsphenamine will suffice.

VAN CREVELD, Amsterdam, Netherlands.

ETIOLOGY OF ACUTE NEPHRITIS. P. FORMYNE, Nederl. tijdschr. v. geneesk. **90**:282 (April 13) 1946.

In this clinical lecture the author discusses the etiology of acute nephritis in Amsterdam in 1945. He states that provisionally no definite explanation can be given.

VAN CREVELD, Amsterdam, Netherlands.

Nervous Diseases

THE TREATMENT OF INFLUENZAL MENINGITIS. MARGARET H. D. SMITH, PAUL E. WILSON and HORACE L. HODES, J. A. M. A. **130**:331 (Feb. 9) 1946.

This report covers the 28 patients with influenzal meningitis seen at Sydenham Hospital (Baltimore) since 1941. The season incidence was highest in November, December and January. The age incidence was between 3 months and 6 years, with the great majority in the younger age group. Twenty-seven patients had infection with Hemophilus influenzae, type B. In the remaining case the organism could not be typed.

All patients received sulfonamide therapy. A blood level of 8 to 12 mg. for sulfadiazine and of 3 to 6 mg. for sulfapyrazine was sought. Both drugs were effective. Both were continued for two weeks after clinical cure.

The 27 patients with the type B infection received specific therapy with rabbit serum. The dosage was increased as the study progressed so that patients with severe disease were given initial doses of 125 to 150 mg. Twenty-five received serum intravenously and 2 intramuscularly with good results. Serum was not administered intrathecally. Daily assay of patient's serum was done to determine the need for more serum. Immediate reaction to serum was encountered in 2 patients; delayed reaction was common.

Twenty-one patients recovered without sequelae; of these 5 were under 9 months of age. One other patient has since been found to be well. Two patients had residual spasticity and 2 severe damage of the brain. Two patients died. Early diagnosis and intensive early treatment are cited as the reason for these strikingly good results.

BAIRD, Wauwatosa, Wis.

Diseases of the Genitourinary Tract

PROPHYLAXIS OF TESTICULAR TORSION. P. J. ALLAART, Nederl. tijdschr. v. geneesk. **90**:164 (March 2) 1946.

In the majority of the cases of testicular torsion operative treatment is necessary. If the circulation returns after the torsion, one may try to retain the testis and to fix it in position. If the circulation does not return, semicastration must be performed. Exploration of the other nonrotated testis with eventual fixation, in accordance with the theory of Bailey (1936), is of utmost importance to preserve spermatogenesis.

VAN CREVELD, Amsterdam, Netherlands.

HYDREMIA IN ACUTE NEPHRITIS. E. LOPES CARDOZO, Nederl. tijdschr. v. geneesk. **90**:329 (April 20) 1946.

In the systematic investigation of the blood of 18 patients suffering from acute nephritis the author's attention was drawn to the fact that in the very beginning of the disease, which usually is accompanied by edema, the hemoglobin content of the blood and the protein content of the serum always were low. This made the dilution of the blood in this stage of the disease probable. When as a result of restriction of fluid and withholding of salt the edema had disappeared—usually within a fortnight—hemoglobin and serum protein often proved to be normal again, When the edema had disappeared the plasma volume usually was more or less decreased. From these observations the author provisionally concluded that the edema at the beginning of acute nephritis is combined with and perhaps also partly depends on a dilution of the blood. The cause of the hydremia is anuria or oliguria by which water and salt are excreted insufficiently. The practical consequences for the treatment are that administration of water and salt should be restricted until the edema is excreted by an improved diuresis.

VAN CREVELD, Amsterdam, Netherlands.

CASE OF "ANURIA" WITH SOME REFLECTIONS ON A RATIONAL MODERN TREATMENT OF ANURIA. G. VAN HOUTUM, Nederl. tijdschr. v. geneesk. **90**:369 (April 27) 1940.

The author gives the history of a boy 2 years old in whom decapsulation of the kidney was performed on both sides for anuria, which had developed in the course of an acute attack of nephritis after scarlet fever. The boy recovered, and eighteen years later still was in perfect condition.

The author discusses the effect of decapsulation and of the modern treatment of anuria by temporary suppression of the splanchnicus conduction as recommended by Chauvin and others.

VAN CREVELD, Amsterdam, Netherlands.

OPERATIVE CURE OF ECTOPIA OR EXSTROPHIA VESICAE URINARIAE. M. N. ROEGHOLT, Nederl. tijdschr. v. geneesk. **90**:440 (May 11) 1946.

The author surveys the present operative treatments for displacement of the bladder and reports on a case in a boy of 4 years. A urethra, made of a piece of intestine (ileum), was placed between the bladder (closed by operation) and the sphincter ani.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

VITAMINS AND HORMONES IN NUTRITION: II. ENDOCRINE DYSCRASIA. BENJAMIN F. SIEVE, Am. J. Digest. Dis. **13**:80 (March) 1946.

From 200 cases of endocrine dyscrasia with attendant vitamin deficiency 6 cases are reported in detail. The ages of the patients, sex, histories, symptoms and physical and laboratory findings are all different. The diagnoses were made by deduction. The hormones used were thyroid, a hormone like that of the anterior lobe of the pituitary, androgen, estrogenic substances, estrone and lutein. Treatment was aimed at the complete replacement of deficiencies in the hormones and the vitamins.

KIMBALL, Evanston, Ill.

THE INFLUENCE OF TESTOSTERONE PROPIONATE ON THE BLOOD PICTURE. G. A. OVERBEEK, Nederl. tijdschr. v. geneesk. **90**:166 (March 2) 1946.

Little is known about the influence of the male hormone on the blood picture. In experiments with guinea pigs the author found an increase of the number of erythrocytes after injections of testosterone propionate. The same effect was often noted in castrated female Rhesus monkeys.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Muscles, Bones, Joints and Lymph Glands

MYATONIA CONGENITALIS: CASE REPORT. G. L. HALLEZ, Arch. franç. de pédiat. **3**:91, 1946.

Considerable discussion has been aroused in recent years concerning the clinical manifestations of myatonia. The author agrees with the opinions of J. Cathala, recently published, which embrace three types of this condition: (1) acute myatonic states, transitory and curable, such as those found in rickets and established as an entity by Marfan (other conditions which may produce a comparable chain of symptoms are acrodynia, certain muscular hypotonias of endocrine origin and solitary muscular hypotonias of infants, described by Lelong in 1935); (2) congenital myatonia appearing shortly after birth in infants showing mongolism and in others exhibiting the even more infrequent syndrome of atonic astasia—abasia—described by Förster in 1910, and (3) chronic familial amyotrophia of spinal origin, first reported by Werdnig in 1891, and later by Hoffmann in 1893. Another type under this classification is the congenital myatonia of Oppenheim (1900). Observations on a case in the last category are reported at great length in this monograph.

AMESSE, Denver.

SMALL (WRESTLER) SYNDROME OF DE LANGE. ADA MIDDELHOVEN, Ann. pædiat. **166**:283 (June) 1946.

The case history is given of an infant aged 10 months, presenting the "wrestler" type of de Lange, which consists of congenital muscular hypertrophy, extrapyramidal motor disturbances and idiocy. This is the second case observed since de Lange recognized this complex of symptoms as a morbid entity. Thyroid medication instituted to eliminate a factor of hypothyroidism claimed by French pediatricians proved to be entirely unsuccessful. A review of the literature is included.

AUTHOR'S SUMMARY.

TWO SPECIAL CASES OF CONGENITAL DEFECTS OF THE MUSCLES. J. LUTEN, Nederl. tijdschr. v. geneesk. **90**:169 (March 2) 1946.

A case is described in which the following muscles were absent on both sides: the deltoid, the pectoralis major, the serratus anterior and parts of the erector trunci in the lumbar part, whereas the orbicularis oris was retarded in development.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Eye

WHAT IS ORTHOPTICS? WALTER B. LANCASTER, J. A. M. A. **130**:407 (Feb. 16) 1946.

Orthoptics is the art of teaching a patient how to use his eyes properly. It deals with defective habits of seeing, defects of binocular vision and defects of ocular motility. The aim of orthoptics is not primarily to strengthen muscles but to teach better control and coordination and better reflex response.

Heterophoria occurs when there is deviation of the covered eye when the uncovered eye fixates. It is usually mild and corrected reflexly by fusion. Patients with severe heterophoria may be treated surgically, by glasses containing prisms or by orthoptic training to increase the amplitude of fusion. All three methods are often needed and should be used together.

Suppression, the commonest orthoptic disability, occurs when a child ceases to use one eye. Usually he does this to eliminate diplopia caused by excess convergence. Suppression can be cured only by orthoptics. Anomalous convergence or makeshift binocular vision is that in which a patient creates a substitute fovea

in the deviating eye, suppressing the image received on the true fovea. Special difficulties such as those associated with learning to read need special orthoptic treatment.

An orthoptic technician should have a thorough knowledge of the development and function of the eye. Intelligent skill is more important than many elaborate "automatic" machines.

BAIRD, Wauwatosa, Wis.

OCULAR LESIONS IN BESNIER-BOECK-SCHAUMANN DISEASE: SIGNIFICANCE FROM POINT OF VIEW OF DIAGNOSIS AND ETIOLOGY. H. J. M. WEVE, Nederl. tijdschr. v. geneesk. **90**:8 (Jan. 1); 42 (Jan. 19) 1946.

This is a careful study as to how far sarcoidosis is distinguished from those diseases of the eye described as tuberculous. Exclusion of tuberculosis is not sufficient; it is necessary that another virus be demonstrated to be an etiologic factor. The author concludes that provisionally one must assume that in Boeck's disease not only the host, but also the micro-organism, possesses properties by which it is distinguished temporarily, or perhaps permanently, from the common tubercle bacillus.

VAN CREVELD, Amsterdam, Netherlands.

Skin Diseases; Allergy

DESENSITIZATION TO INSECT BITES. ALEXANDER HATOFF, J. A. M. A. **130**:850 (March 30) 1946.

One hundred and twenty-nine children were given injections of 1 to 5,000 polyvalent flea antigen in an effort to lessen their sensitivity to flea bites. Children up to 5 years of age received 0.1 cc. for the first dose and then two doses of 0.2 cc. Older children received a first dose of 0.2 cc. followed by five doses of 0.4 cc. The ages ranged from 2 months to 11 years. One hundred children (78 per cent) benefited from the injections. Six patients (5 per cent) received equivocal benefit. Twenty-three (17 per cent) failed to benefit.

BAIRD, Wauwatosa, Wis.

DELAYED SERUM SICKNESS REACTION TO PENICILLIN. EVERETT J. GORDON, J. A. M. A. **131**:727 (June 29) 1946.

Three patients who received penicillin intramuscularly for nondermatologic conditions had a delayed reaction. This was characterized by (1) delayed appearance, (2) severe malaise with mild fever and moderate tachycardia, (3) severe intense spreading urticaria, (4) arthralgia with serous effusion, (5) exfoliative dermatitis of the palms of both hands and (6) self-limited course of seven to ten days regardless of treatment.

BAIRD, Wauwatosa, Wis.

FATAL ANAPHYLACTIC SHOCK: OCCURRENCE IN IDENTICAL TWINS FOLLOWING SECOND INJECTION OF DIPHTHERIA TOXOID AND PERTUSSIS ANTIGEN. JACOB WERNE and IRENE GARROW, J. A. M. A. **131**:730 (June 29) 1946.

The second injection of diphtheria toxoid and pertussis antigen given to 10 month old twin boys one month after the first injection of the same material led to the appearance of shock within a few hours and death within twenty-four hours. Postmortem examination showed widespread lesions suggesting arterial spasm and increased endothelial permeability and indicating the basic role of vascular injury in a hypersensitive state.

Postmortem cultures were negative. Examination of the material remaining in the vial used in immunizing the children showed it to be satisfactory. The family history was positive for allergy in that the father of the twins had had two episodes suggesting angioneurotic edema.

BAIRD, Wauwatosa, Wis.

THE DIFFERENTIAL DIAGNOSIS AND TREATMENT OF SCABIES IN EARLY INFANCY. A. P. JORDAN, Pediatriya **3**:59, 1944.

The author claims that the diagnosis of scabies in newborn and young infants is not always an easy one for the following reasons: First, the scabies dermatitis in young infants is often eczematoid in character; second, the scabies burrows, contrary to what would be expected, are not prominent, and, third, the fingers and wrists, which are the favorite locations of scabies burrows in adults, are usually spared in young infants. The author claims that the trunk is by far the most common location for the scabies burrows in young infants.

Scabies dermatitis in young infants usually appears in the form of small vesicles followed by the formation of small nodules and pustules. The rash shows a predilection for the trunk, especially the back, the buttocks and the extensor surfaces of the lower extremities. The chin and the lower half of the face are a common location in breast-fed infants who become contaminated during nursing. The eczematoid form of scabies in young infants may have to be differentiated from a mild infantile eczema, and the characteristic location of the scabies dermatitis is one of the most important differential diagnostic points. Furthermore, scabies is a relatively rare disorder in the young infant, as may be judged from the author's experience at a large children's clinic in Moscow, where for every 10 cases of infantile eczema the author saw only 1 case of scabies.

As an ideal treatment for scabies in young infants the author considers a 10 per cent preparation of balsam of Peru. Next best is the following prescription: sublimed sulfur, 5.0; pine tar, 3.0, and petrolatum, 100.0. Zinc oxide ointment may be substituted for half of this quantity of petrolatum in the presence of an extremely sensitive skin. It is advisable to apply the ointment twice daily, to be followed by a bath on the fourth day of treatment. Not more than two weeks are usually required for a complete cure with this form of therapy. In the rare event of a development of a sulfur dermatitis the author suggests the use of the following preparation: zinc oxide, 10.0; aromatic castor oil 10.0, and olive oil, 40.0.

BODER, Los Angeles.

Surgery and Orthopedics

THE SURGICAL TREATMENT OF FUNNEL CHEST. CHARLES W. LESTER, Ann. Surg. **123**:1003 (June) 1946.

Funnel chest is a deformity of the sternum characterized by a funnel-shaped depression of the sternum with the apex at the ziphoid. The deformity is generally considered to be congenital and hereditary. It is due to a short central tendon of the diaphragm.

The effect of the deformity on the thoracic viscera is that of compression. The volume of the lungs is decreased in proportion to the deformity. The effect on the heart is proportionate to the pressure on it and not necessarily to the degree of deformity. During inspiration the sternum moves backward and the entire funnel deepens, while during expiration the movement is in the opposite direction.

In infancy, when the deformity is in a reversible stage, a simple operation will correct it. Later, when the deformity has become fixed, a more complicated operation is necessary which must not only release the diaphragmatic pull but must also correct the long deformity which has resulted from this pull. Operation results in a high percentage of satisfactory results. Eight cases are reported.

BANTIN, Omaha.

SEVERE BURNS FROM INFLAMMABLE COWBOY PANTS. W. EMORY BURNETT and H. TAYLOR CASWELL, J. A. M. A. **130**:935 (April 6) 1946.

Severe burns of the lower extremities are recorded in 3 boys whose cowboy pants bearing the trade name "Gene Autry" were completely ignited on trivial exposure to fire.

"Material made into clothing should be thoroughly tested as to inflammability before being offered for sale to the public."

BAIRD, Wauwatosa, Wis.

Miscellaneous

SEQUELAE FOLLOWING ORAL AND TOPICAL USE OF PENICILLIN. LOUIS KLEINFELD, New York State J. Med. **46**:915 (April 15) 1946.

The general opinion emphasizes the lack of untoward symptoms from penicillin other than urticaria. But Kleinfeld has seen 2 patients who had definite and disturbing symptoms. He reports 6 patients who came under observation. The first swallowed three enteric-coated tablets of 25,000 units each. There were violent cramps and distention. One hour later the patient took three more. No ill effects were reported. The next day one 25,000 unit tablet caused a return of the discomfort. A second patient had similar symptoms following similar ingestion of penicillin tablets buffered with sodium citrate. Patient 3 was given penicillin orally and intramuscularly for "sore throat." Membranous patches appeared in the pharynx which required "weeks to wear off." Penicillin drops were then instilled into the nose. Stomatitis followed an acute attack of rhinitis with discrete red lesions on the hard palate. Glossitis was a later incident. All symptoms cleared up promptly when the penicillin was stopped. Case 4 was reported verbally by Dr M. C. Myerson. The patient had ulcers on the pharynx, tongue and lips after having been given tablets orally over a four day period. Improvement took place within twenty-four hours after administration of penicillin was stopped. Gingivitis in case 5 with stomatitis occurred after oral administration, but cleared up in one week. Patient 6 had a pustular dermatitis in the nares after penicillin ointment was used, but the condition cleared up promptly after the use of penicillin was stopped. The author suggests that impurities may have been mixed in with the penicillin, especially formaldehyde in case 1, which coated the capsule, but decides finally that "penicillin itself was the common factor."

VOORHEES, New York. [ARCH. OTOLARYNG.]

ANTIBIOTIC ACTIVITY OF EXTRACT OF WESTERN RED CEDAR HEARTWOOD. CHESTER M. SOUTHAM, Proc. Soc. Exper. Biol. & Med. **61**:391 (April) 1946.

Inasmuch as certain woods are highly resistant to decay and hot water extracts of western red cedar yield antibiotics to wood-destroying fungi, the author conducted studies with such extracts on micro-organisms pathogenic to man. Crude filtrate of freshly made cedar sawdust with distilled water was prepared, being simmered for forty-eight hours. The material was not well standardized. The inhibition found was due to stasis, not to death of the organisms. The susceptibility of the micro-organisms was unrelated to morphology or gram-staining reaction. The antibiotic activity was not lost by boiling or change in p_H, or inactivated by urine or gastric residue, but was inactivated by blood, serum and cystine. No activity in vivo against infection has been demonstrated, but large doses of the extract did not cause illness or death of rabbits.

HANSEN, Galveston, Texas.

POISONING WITH DULCIN: REPORT OF A CASE. J. PRESMAN and J. LUTEN, Nederl. tijdschr. v. geneesk. **90**:261 (March 30) 1946.

A boy nearly 3 years old took 200 tablets, each containing 12 mg. of dulcin (paraphenetolcarbamide), which corresponded to 165 mg. per kilogram of body weight. Distinct gastrointestinal symptoms developed; there were further slight symptoms referable to the central nervous system and probably also a temporary methemoglobinemia.

VAN CREVELD, Amsterdam, Netherlands.

Book Reviews

Mongolism and Cretinism: A Study of the Clinical Manifestations and the General Pathology of Pituitary and Thyroid Deficiency. By Clemens E. Benda, M.D. Price $6.50. Pp. 310, with 48 tables and 103 figures. New York: Grune & Stratton, Inc., 1946.

This book, written by the director of the Wallace Research Laboratory, is the result of ten years' continuous research on the subject. It contains the records of 300 patients of all ages who were examined, and of many more who were observed, during the ten year period. Through the performance of 50 autopsies, it was possible to study every aspect of the disease from birth to death, the occurrence of which ranged from the age of 2 days to over 30 years. These data are contained in the opening chapters on "Physical Characteristics," "Mental Development," "Nervous System," "Endocrine Pathology," "General Pathology," "Growth and Development of the Skull and Bones," "X-Ray Studies" and "Hematology and Biochemistry."

These observations offer an amount of material which is far greater than that to which those studying the condition have hitherto had access, and the author has done full justice to the subject in his excellent measurements, roentgenologic observations and biochemical and psychologic studies. By far the most valuable are the pathologic studies of the pituitary gland, from which the author develops his thesis that mongolism is the result of a pituitary dysfunction.

While these observations on the dysfunction of the pituitary gland are of exceptional interest, the author has placed too much stress on the thesis that this is the cause of mongolism. One must remember that as yet this is far from proved. I believe that the author has weakened the entire text by this endeavor, as well as by including cretinism in a parallel discussion with these observations on mongolism. Nothing particularly new has been added to the knowledge of cretinism, and the observation that cretinism is known to be a disorder of a gland, the thyroid, does not at all prove that mongolism is a disorder initiated by dysfunction of the pituitary gland. This the reader will have to judge for himself.

I believe that the two final chapters are also unfortunate. In "Prevention of Mongolism," which might be taken by lay readers as a definite statement, great stress is laid on the age factor of the mother, the significance of which, of course, has been known for many years. Percentage studies of the age incidence of mongolism and vague metabolic tests will serve only to cause uncalled-for fear in every mother who is bearing a child near the end of the child-bearing period. The final chapter, "Principles of Treatment," states that "the therapy of choice is an efficient pituitary treatment." One can imagine this remark being seized on by lay writers who have not taken the trouble to read further that "unfortunately this treatment is not available at present."

However, these statements in no serious way detract from the value of this book. It is an excellent piece of work, well written and well put together. The printing is excellent, and the charts and photographs are good and well chosen. This book should be in the library of all those interested in this subject.

Modern Development of Chemotherapy. By E. Havinga, H. W. Julius, H. Veldstra and K. C. Winkler. Price, $3.50. Pp. 175; no illustrations. Amsterdam: Elsevier Publishing Co., 1946.

This book is one of the first reports from the nations oppressed by Nazi occupation. The editors explain in a foreword that this series of "Monographs on the Progress of Research in Holland During the War" was planned during wartime and the material kept secret up to the present. Publication at the earliest possible moment after the war did not permit the inclusion of references to worldwide

literature and forced the authors to report mainly the results of their own investigations.

The subject treated is the group of sulfonamide compounds and the discussion in the various chapters is in minute detail. Any investigator in the field of chemotherapy in general and of the sulfonamide drugs specifically will find it most interesting to read of the experimental work done in the Netherlands and of the theories brought forth by the authors. The mechanism of action is discussed from the bacteriologic and the physicochemical viewpoint, and much consideration is given the theory of antagonism of *p*-amino acids. The chapter on chemical investigation lists all the sulfanilamide derivatives known to the authors and briefly discusses their qualifications. Another chapter deals with the pharmacologic, immunologic and clinicotherapeutic investigations carried out in the Netherlands. From the point of view of the practicing physician it is regrettable that not more space is allotted to the clinical part, which, indeed, consists only of short comments on the action of the drugs on various organisms and of brief references to the literature. The shortness of this chapter and the extensive discussion of the laboratory aspects make the book valuable for the investigator only.

The last chapter in the book is on mycotherapy and antibiotic substances. It is interesting to note that in the Netherlands investigation on the antibiotic action of certain micro-organisms was begun independently of, and in a different direction from, that taken by the Anglo-American groups. Van Luijk is mentioned as the man who studied the antibiotic action of micro-organisms on plant parasites. He called his product "expansine." In experimental work on animals the substance was found too toxic for internal use. Clinically, external application, especially in treatment of fungous infections, showed some favorable results, however.

There are now twenty-four volumes, representing various fields, in this series of monographs. New volumes are announced to follow.

Genetics, Medicine and Man. By H. J. Muller, Ph.D.; C. C. Little, Sc.D., and L. H. Snyder, Sc.D. Price, $2.25. Pp. 153; 29 figures, 8 tables. Ithaca, N. Y.: Cornell University Press, 1947.

This book comprises six lectures delivered at Cornell University in 1945 under the title "Messenger Lectures on the Evolution of Civilization." The first two lectures, by H. J. Muller, deal with genetic fundamentals. In nontechnical language, the cytologic basis of the reproductive process and of the distribution of the genetic material among the cells of the body is explained. Some interesting paragraphs are devoted to fundamental problems which are usually not stressed in textbooks of genetics: How genes, alike in all parts of the embryo, cause the parts to differentiate; what the gene does chemically, and how the gene reproduces itself. The causes and the mechanisms of gene mutations are discussed. The modern geneticists' view of the process of evolution is briefly described and interpreted.

C. C. Little contributes chapters entitled "Parental Influence" and "Growth and Individuality." The relation of mammalian genetic experiments to problems of human medicine is pointed out, and the reader is led to recognize the opportunities offered to the medical research worker by the wealth of mammalian genetic material. Pediatricians with broad biologic interests will find these two chapters stimulating reading.

Some aspects of human heredity are discussed by L. H. Snyder. The difficulties in the collecting of genetic data in man are emphasized, the relative roles of heredity and environment in the production of human traits and diseases are explained and some practical applications of human genetics are cited. That prognosis, diagnosis and preventive measures may be benefited by knowledge of the family history and of the mode of inheritance in certain pathologic conditions is stressed. A discussion of the mutant gene in man includes an exposition of the spatial relations of the gene (location on an autosome or on the various parts of the sex chromosomes) and of its physiologic relations (penetrance, expressivity

and viability). The ontogenetic relations of the gene (interaction of genes in the organism) and its phylogenetic relations (frequencies of genes and genotypes) are explained.

Allergy. By Erich Urbach, M.D., and Philip M. Gottlieb, M.D. Second edition. Price, $12. Pp. 968, with 411 illustrations. New York: Grune & Stratton, Inc., 1946.

This is an impressive book; it weighs 5 pounds, 6 ounces (2,438 Gm.). It contains 411 illustrations of superior quality and 3,325 references. It is the most complete review of allergy in existence.

The subject matter is divided into three sections: (1) the fundamentals of allergy, (2) etiologic agents of allergic diseases and (3) symptoms and therapy of allergic diseases.

Section 1 contains 232 pages of critical discussion of the basic principles of hyposensitiveness and hypersensitiveness, the mechanism of allergy, the nature of antigens and antibodies, the relation of animal anaphylaxis to human allergy, the diagnosis of allergic diseases and the principles of treatment. Although presenting some views and using nomenclature somewhat different from those of most allergists in this country, this section is well written, and could have been written only by a tireless and thoughtful student who is thoroughly acquainted with all the important work that has been done on the subject both here and in Europe. This section will be of considerable value to the allergist; it is not suitable for those who do not devote most of their time to the study of allergy.

Section 2 discusses in detail the innumerable inhalants, ingestants, injectants, contactants, infectants and physical agents which may produce allergic sensitization. This section is invaluable for reference, and in the reviewer's opinion is the best part of the book.

Section 3 is concerned with the various diseases which are known to be or possibly thought to be caused by allergy. The portion devoted to hay fever is adequate and consists of 43 pages. Six pages are devoted to discussion of the oral method of hyposensitization with pollen extracts or pollen "propeptans." The authors apparently use this method of treatment extensively. Most allergists have come to the conclusion that it is of little value.

The section on allergic cutaneous diseases contains many excellent and unusual illustrations, which add materially to its value. Contact dermatitis and neurodermatitis are adequately discussed. Most pediatricians and allergists would not agree with the authors' statement that an underlying nutritive allergy is demonstrable in all cases of papular urticaria in infants and young children. "In 15 cases, although it was impossible to identify the nutritive allergens, administration of polypropeptans resulted in complete cure." Several rather extensive studies on papular urticaria have appeared in the last ten years, and the one thing that has been brought out clearly is that it is hardly ever possible to demonstrate that specific food sensitivity has anything to do with it.

There is a short chapter on allergy in the newborn, in infancy and in childhood. The amount of space devoted to this is in proper proportion to the rest of the subject matter in a book devoted mostly to allergy in the adult. It is too incomplete to be of much value to the pediatrician.

This book is rather a review of allergy than a record of the authors' personal experience, although they have undoubtedly had a large experience. As a review of allergy it is very complete; as a guide for the practitioner in definite treatment it is not so satisfactory, and methods of treatment are recommended which are not in approved use.

Much has been written on allergy that is of little or no value, and many methods of treatment have been enthusiastically advocated by some persons which have proved worthless in the hands of others. If any drug, any method of treatment is good in medicine, there is nothing more certain than that in a short time it is completely and unequivocally accepted by almost all physicians—insulin, liver

extract for pernicious anemia, quinine, tetanus and diphtheria toxoid, the sulfonamide compounds and penicillin. In this book too much attention is given to theories and to therapeutic procedures which have never been accepted, and never will be. In spite of these defects, it is valuable, especially as a reference book for the serious student of allergy. It is not recommended for the beginner, for the general practitioner or pediatrician, or for any one whose main interest is other than allergy.

Dentistry, An Agency of Health Service. Edited by Malcolm Carr, D.D.S. New York Academy of Medicine. Price, $1.50. Pp. xxiv + 219; no illustrations. New York: The Commonwealth Fund, Division of Publications, 1946.

This book was prepared by many authors, under the direction of Dr. Carr, and published as part of the series on "Medicine and the Changing Order." There is a brief but accurate chapter on the historical development of the dental profession; another on undergraduate and graduate education in dentistry, and some carefully prepared statements on the present status of dental schools and hospital dental service, as well as an analysis of the present status of dental service in the United States.

Throughout the book emphasis is placed on the scientific and technical progress which has been made in dentistry and the urgent need at present of improving the procedures in preventive dentistry. The dental profession appears to be on the threshold of discovering methods for controlling, if not entirely preventing, dental caries in children; but the fact remains that at the present time the teeth of the children of this country are receiving too little attention and the injuries which occur in childhood result in serious malformations and deformities in adult years.

The book does not offer a complete solution to these problems, but it does give a rather accurate and careful analysis of the present status of dentistry, dental education and the public health needs of the present day.

The Premature Baby. By V. Mary Crosse, M.D., D.P.H. No price listed. Pp. 156, with 14 illustrations. Philadelphia: The Blakiston Company, 1945.

Dr. Crosse has presented a good description of the premature as compared with the full term infant. Concisely, she has detailed simple equipment and methods for the adequate care of a premature baby in the home or in the hospital. She shows graphically the effect of these measures in terms of number of lives saved over a period of twelve years in the City Maternity Home, Birmingham, England. The complications of prematurity, as well as their prevention and treatment, are well described. The feeding methods recommended are those in common use in this country. However, the substances to be used and their dilutions and quantities are somewhat at variance with the opinion of many physicians in this country who have had wide and highly successful experience in handling premature infants.

This book should prove of practical value to the pediatrician, obstetrician, general practitioner or nurse who has not had broad experience in the care of premature infants.

The 1946 Yearbook of Pediatrics. Isaac A. Abt and Arthur F. Abt, Editors. Price, $3.75. Pp. 449, with many illustrations. Chicago: The Yearbook Publishers, 1947.

As the title implies, this volume constitutes a review of the major contributions to the field of pediatrics during the year prior to its publication. The editors have executed the difficult task of choosing their subject matter in a manner which admirably covers an abundant literature. However, the reviewer is of the opinion that inclusion of "Growth and Development" as one of twenty main sections would have been desirable, because of the fundamental importance of these subjects to all pediatricians.

The reader is stimulated to critical appraisal in his reading by the frequent appearance of succinct editorial comment following the discussion of individual papers.

References are made to source material throughout, though, for obvious reasons, more complete bibliographies do not appear. Any student of pediatrics can gainfully review and refresh his knowledge of the pediatric literature between the covers of this book and have suggested to him numerous new technics and practical therapeutic approaches.

The Personality of the Preschool Child. By Werner Wolff, Ph.D. Price, $5. Pp. 301, with 118 illustrations. New York: Grune & Stratton, 1946.

"It is almost as if the child and the adult live on two different planets." In this manner the author emphasizes the growth and development of a child, and the difference between the reactions of children and of adults. Feeling that most psychologists (and psychiatrists) proceed from adult viewpoints the author has attempted to explain the personality reactions of the child himself. He has sought explanations of child behavior in terms of the child's own imagination and expressions, whether they are in speech, play or drawings. The author considers the child's own interpretations of his drawings, for instance, more important than an adult's interpretation of them. In growing up the child lives in bewilderment, trying to find out about himself and those around him.

In succeeding chapters the author points out the difference between the mind of the child and that of the adult; the emotions of the child and those of the adult; the social relationship, especially in the family; the child's concept of reality, especially stressing imagination; the preschool child as an individual; the child's feeling of security; intelligence of the preschool child, including sense of rhythm and the factor of relationships as an innate factor of personality; methods of judging expressive behavior of preschool children; principles of childreu's art; the educational bridge between the two worlds—of children and of adults; and methods of child psychology.

The whole book stresses the importance of trying to understand the growth of the mind. The book is well written, principles are clearly expressed and the material is well chosen.. This book should be interesting and instructive to any one interested in the dynamics of growth.

Essentials of Pediatrics. Philip C. Jeans, A.B., M.D.; Winifred Rand, A.B., R.N., and Florence G. Blake, R.N., M.A. Fourth edition. Price, $3.50. Pp. 627, with 86 illustrations. Philadelphia: J. B. Lippincott Company, 1946.

The fourth edition of this popular text has been completely rewritten and embodies much new material taken from recent pediatric advancement. The contents have been arranged into units to conform with the recommendations of the curriculum for schools of nursing prepared by the National League of Nursing Education.

The text is divided into five units. The first unit deals with orientation, the introduction to pediatric nursing and preventive pediatrics.

Unit two discusses growth, development, hygiene and the training of the infant and child. In this unit the growth charts based on the Iowa City data are presented.

Unit three is devoted to general nursing care in the hospital and home.

Unit four is concerned with nursing care of diseases of children. This is the largest unit, and it includes diseases of the newborn, diseases of the various systems, communicable diseases, rheumatic fever, rabies, tetanus, brucellosis, recurrent vomit-

ing, acidosis and alkalosis, acrodynia and allergy. The chapters on diseases of the eye, of the blood and of the glands of internal secretion appear for the first time and add to the completeness of the book.

Unit five presents nutrition and nutritional diseases.

The authors point out that it is necessary for a competent pediatric nurse to have training in the principles of child guidance as well as in children's nursing technic. The discussions of nursing care have been written to fulfil this need. A new co-author, Florence G. Blake, has aided in the presentation of this material.

All who read this book will receive much practical pediatric instruction. It is to be recommended especially to all student and pediatric nurses and to the faculties of schools of nursing.

Daytime Care: A Partnership of Three Professions. Findings of the Tri-Profession Conference on Day Care of the Child Welfare League of America, Inc. Price, 35 cents. New York: Child Welfare League of America, Inc., 1946.

Aware of the many problems throughout the country in providing adequate care for children not only during the war years but in the immediate postwar period, the Child Welfare League of America arranged a conference to discuss this subject. Out of the conference evolved a procedure that concerns professional and lay groups interested in the welfare of the child. Certain premises were adopted to justify the position taken by the league in this report.

Daytime care of children should aim to strengthen family life and help our children, individually, or in groups. The coordinated skills of education, medicine and case work should be available when needed. Daytime care for children away from their own homes is provided through a variety of services. These include public and private schools, day nurseries, child care centers, family day care, homes, and various independent facilities. The integration of the three skills of education, medicine and social work is needed in any one of these services if the best interests of the child and his family are to be served.

The educational services in child care centers should include: (1) Guiding each child in his group experience. Such guidance is based on a knowledge of child development and the ability to apply its principles to the particular group situation for the maximum benefit of each child. (2) Setting up the environment for satisfactory group living. (3) Planning schedule and program to provide experience for individual growth and well-being. (4) Developing good parent-staff relationships. (5) Sharing responsibility for the adequacy of services to all children.

The health services in child care centers should include: (1) education of the parent concerning the health needs of the child, (2) education of the staff by the pediatrician, (3) evaluation of plant and equipment from the point of view of health, sanitation and safety, (4) evaluation of the adequacy of the total program from the health standpoint, (5) evaluation of the health of children and staff members, with recommendations for adjustments or treatments indicated, (6) control of infections among staff and children, (7) management of accidents, (8) referral for special services when needed and (9) keeping of medical records.

The personnel concerned in health services should consist of the local health officer, the nurse, the pediatrician, the staff member, the nutritionist and the psychiatrist or psychiatric service. The case worker's responsibilities should include applications, continuing relationships and termination of the service.

The report recommends training programs for child care center personnel, both professional and staff training. This carefully planned report is highly recommended for any group sponsoring nursery schools or daytime care of children. A well regulated program is outlined in detail.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: New York. Time: July 14-17, 1947.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Pan American Congress of Pediatrics

President: Dr. Felix Hurtado, Habana, Cuba.
Place: Mayflower Hotel, Washington, D. C. Time: July 9-12, 1947.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff, Hospital for Sick Children, Great Ormond St., London, W. 1.

Danish Pediatric Society

President: Prof. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

NEDERLANDISCHE VEREENIGING VOOR KINDERGENEESKUNDE

President: Dr. J. L. Keyzer, 114 St. Josephstr., Tilburg.
Secretary: Dr. H. Reerink, 2B Paul Krugerstr., Arnheim.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASES IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD BOLIVIANA DE PEDIATRIA

President: Dr. Ernesto Trigo Pizarro.
Secretary: Dr. Carlos Ferrufino, Casilla 272, La Paz, Bolivia.
Place: La Paz, Bolivia.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clínica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD DOMINICANA DE PEDIATRIA

President: Dr. Alberto Peguero, Ciudad Trujillo, R.D.
Secretary-Treasurer: Dr. Jaime Jorge, Ciudad Trujillo, R.D.
Place: Children's Ramfis Hospital. Time: 8 p. m., last Thursday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Luis Berlanga Berumen, Bucareli No. 85, Altos, Mexico.
Secretary: Dr. Jésus Alvarez de los Cobos, Ignacio Mariscal 124, Mexico.

SOCIEDAD DE PEDIATRÍA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba, Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina.
Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

Sociedad Venezolana de Puericultura y Pediatria

President: Dr. Pastor Oropeza, Caracas.
Secretary: Dr. Carlos E. Castillo, Hospital Municipal de Niños, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

Société de Pédiatrie de Paris

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

Swedish Medical Society, Section for Pediatrics and School Hygiene

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

Uruguayan Society of Pediatrics

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Oscar Reiss, 2200 W. 3d St., Los Angeles.
Secretary: Dr. Margaret Mary Nicholson, 1801 Eye St. N. W., Washington, D. C.
Place: Chicago. Time: June 21-25, 1948.

American Academy of Pediatrics

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.

American Hospital Association, Massachusetts Hospital Association

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

American Pediatric Society

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

Canadian Society for the Study of Diseases of Children

President: Dr. Alan Ross, 1414 Drummund St., Montreal.
Secretary-Treasurer: Dr. R. L. Denton, 3534 Ontario Ave., Montreal.

Society for Pediatric Research

President: Dr. Donovan J. McCune, 3975 Broadway, New York.
Secretary: Dr. Robert Ward, Bellevue Hospital, New York 16.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Wesley H. Anderson, 2404 Washington Blvd., Ogden, Utah.
Secretary-Treasurer: Dr. F. M. Kriete, State Capitol, Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. Percy Guy, 502–2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

Northwestern Pediatric Society

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. Jackson L. Sadler, 109 W. Olive St., Ft. Collins, Colo.
Secretary: Dr. Edwin T. Williams, 1850 Gilpin St., Denver 6.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.

STATE

Alabama Pediatric Society

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

Arizona Pediatric Society

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.

Florida State Pediatric Society

President: Dr. James R. Boulware, Lakeland.
Secretary: Dr. Hugh A. Carithers, 2000 Park St., Jacksonville 4.
Place: Concurrent with state association convention and fall meeting.

Georgia Pediatric Society

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. David Gaberman, 1179 Allyn St., Hartford, Conn.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Gerard N. Krost, 2376 E. 71st St., Chicago.
Secretary: Dr. Frederick H. Maurer, 331 Fulton St., Peoria 2.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.

Louisiana State Pediatric Society

President: Dr. R. V. Platou, 1430 Tulane Ave., New Orleans 13.
Secretary-Treasurer: Dr. Bertha Wexler, 3439 Prytania St., New Orleans 15.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Joseph A. Gilmartin, 3700–5th Ave., Pittsburgh 13.
Secretary: Dr. Carl C. Fischer, 100 W. Coulter St., Philadelphia 44.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. Paul N. Morrow, 1614 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Michael Crofoot, 1407 Medical Arts Bldg., Omaha 2.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Mexico State Pediatric Society

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

North Carolina Pediatric Society

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.

Northern California Pediatric Society

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. J. B. Snow, 625 N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

Tennessee Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellview, Memphis.
Secretary-Treasurer: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Time: Second Monday in April.

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Baltimore City Medical Society, Pediatric Section

Chairman: Dr. Charles O'Donovan Jr., 5 E. Read St., Baltimore.
Secretary: Dr. T. Campbell Goodwin, 16 E. Biddle St., Baltimore.

Bronx Pediatric Society

President: Dr. Harry S. Pizer, 1726 Davidson Ave., New York.
Secretary: Dr. Nathan M. Greenstein, 1488 Metropolitan Ave., New York.
Place: Morrisania City Hospital. Time: 8:30 p. m., second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. George E. Brockway Jr., 176 Fenimore St., Brooklyn.
Secretary: Dr. Bernard Benjamin, 845 Park Pl., Brooklyn 16.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, October and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. H. William Elghammer, 2371 E. 71st St., Chicago.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Shirley Hodges, 2703 Oak Lawn Ave., Dallas, Texas.
Secretary-Treasurer: Frances M. Love, 4585 Belfort, Dallas 4.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. George Salmon, 1220 Bartlett St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., last Tuesday of each month

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Knoxville-Oak Ridge Pediatric Society

President: Dr. Henry S. Christian, 205 Medical Arts Bldg., Knoxville, Tenn.
Secretary: Dr. John Eggleston, Oak Ridge Hospital, Oak Ridge, Tenn.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Secretary-Treasurer: Dr. Robert Simonds, 267 S. Beverly Dr., Beverly Hills, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Louis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

Oklahoma City Pediatric Society

President: Dr. J. B. Snow, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Bertha Levy, 1200 N. Walker St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Arthur M. Dannenburg, 235 S. 15th St., Philadelphia 2.
Secretary: Dr. D. Stewart Polk, Rosemont, Pa.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday from October to May, inclusive.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

Richmond Pediatric Society

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. Jerome Glaser, 300 S. Goodman St., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Daniel B. Peeler, 1162 Lake Ave., Rochester 13, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

San Antonio Pediatric Society

President: Dr. Sidney R. Kaliski, 518 Moore Bldg., San Antonio 5.
Secretary-Treasurer: Dr. Edith M. Bonnet, 228 Medical Arts Bldg., San Antonio 5.
Place: Variable. Time: 7:30 p. m., first Tuesday of every month.

Seattle Pediatric Society

President: Dr. Norman W. Murphy, 1300 Madison St., Seattle 4.
Secretary: Dr. David M. Harris, 630 Medical Arts Bldg., Seattle 1.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Donald C. Shelby, 416 N. Bedford Dr., Beverly Hills, Calif.
Secretary: Dr. Harry F. Dietrich, 416 N. Bedford Dr., Beverly Hills, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.